EXHIBIT B

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA

CHARLESTON DIVISION

IN RE: BOSTON SCIENTIFIC CORP., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02326** **MDL 2326** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**
THIS DOCUMENT RELATES TO THE FOLLOWING CASES: **THIS DOCUMENT RELATES TO ALL BOSTON SCIENTIFIC CORPORATION CASES INVOLVING AN ADVANTAGE, ADVANTAGE FIT, LYNX, OBTRYX, SOLYX, PREFYX, PINNACLE, AND UPHOLD**	

GENERAL EXPERT RULE 26 REPORT OF BRUCE A. ROSENZWEIG, M.D.

I am Dr. Bruce A. Rosenzweig, M.D. Any medical opinions rendered in this report represent my opinions, all held to a reasonable degree of medical certainty, and are based on reasonable medical probability and a scientifically reliable method.

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I. QUALIFICATIONS

I am currently an Assistant Professor of Obstetrics and Gynecology at Rush University Medical Center in Chicago, Illinois. I received my MD degree in 1984 from the University of Michigan in Ann Arbor, Michigan. Following graduation from medical school, I completed an Obstetrics and Gynecology Residency at Michael Reese Hospital in Chicago. In 1988, I attended a one year pelvic surgery fellowship at State University of New York in Syracuse, New York. Following that fellowship, I attended a two year Urogynecology and Urodynamics fellowship at UCLA Harbor General Hospital in Torrance, California. After graduating from the Urogynecology fellowship, I became a faculty member at the University of Illinois in Chicago. I started a Urogynecology program at the University of Illinois and also was the residency program director.

In 1998, I went into private practice, and subsequently established a private practice at Rush University Medical Center. I have also worked at John H. Stroger Hospital here in Chicago from May 2003 until November 2010 and Weiss Memorial Hospital as Associate Chair of Gynecology from February 2011 until July 2012. I have published numerous articles and given numerous lectures on the topics of pelvic organ prolapse, urinary incontinence and repair of pelvic organ prolapse. Additionally, I was invited by Ethicon and attended its Gynecare Prolift Training Seminar and TVT Obturator Seminar in Belgium. I was also invited to a Bard Avaulta training seminar in the past. My full qualifications are set forth in my Curriculum Vitae attached to this Report as Exhibit "A".

Throughout my career, I have performed over a thousand pelvic floor surgical procedures, including abdominal sacrocolpopexy, uterosacral suspensions, sacrospinous ligament fixations, native tissue repairs, biological graft repairs and synthetic mesh repairs. I have used numerous synthetic pelvic mesh products, including Ethicon's TVT Classic, TVT Obturator and Prolift. I have performed over 350 surgeries dealing with complications related to synthetic mesh, including the removal of Advantage Mesh slings and Polyform mesh prolapse devices. I have also treated more than 1,200 additional patients with mesh non-surgically.

A copy of my CV and Fee Schedule is attached as Exhibit "A" and a copy of my testimony for the last four years is attached as Exhibit "B". The documents I relied on for this report are contained in Exhibit "C" as well as those documents cited throughout this Report.

II. SUMMARY OF OPINIONS

In formulating my opinions and preparing this report, I reviewed scientific literature, corporate documents from Boston Scientific ("BSC"), documents in the public domain, sample products and depositions of BSC employees. I have also reviewed and relied upon extensive medical and scientific literature concerning these products and other mid-urethral polypropylene mesh slings. All opinions expressed herein are based on my experience, training, knowledge, and the reliance material identified herein. A list of BSC corporate documents and depositions reviewed for this report is attached hereto as Exhibit "B"; all other materials reviewed are listed at the end of this report. All opinions expressed herein are held to a reasonable degree of medical and scientific certainty. I understand discovery is still ongoing in this case, and I reserve my right to amend my opinions if further information is provided to me in any form including, but not limited to, corporate documents, depositions and the expert reports of both Plaintiff and Defense experts. In general, my expert opinions can be summarized as follows:[1]

A. BSC constructed the Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Prefyx, Pinnacle, and Uphold (collectively, "BSC Mesh Products") with polypropylene that is not suitable for permanent transvaginal implantation to stress urinary incontinence of pelvic organ prolapse; the polypropylene degrades over time, causes chronic foreign body reactions, fibrotic bridging, mesh contracture / shrinkage, fraying, deformation, roping, rolling and curling of the mesh;

B. BSC's Mesh Products lack adequate studies to establish safety and effectiveness for permanent human implantation to treat stress urinary incontinence or pelvic organ prolapse. Without the evidence, BSC's Mesh Products are not suitable for permanent implantation because BSC did not consider relevant and knowable problems and complications associated with implanting its products through the vagina and into the pelvic cavity;

C. BSC disregarded prior experience with the Protegen device when manufacturing the Mesh Products;

[1] This is not intended to be an exhaustive recitation of my opinions in this case. The full scope of my opinions is described in further detail in this report.

D. BSC made public claims about the properties and safety of the Mesh Products to physicians and patient through marketing materials that lack support from the available medical and scientific literature;

E. The Directions For Use ("DFU") BSC provided with all Mesh Products do not fully disclose or adequately warn about the Mesh Products' known or knowable risks, adverse reactions, and characteristics;

F. The severe, debilitating, and life-changing complications associated with the Mesh Products outweighed the products' benefits, which are comparable to the benefits with non-mesh interventions ; and

G. BSC polypropylene mesh removal requires a difficult and sometimes impossible surgery with a high likelihood of injuring surrounding tissue.

III. BACKGROUND AND TREATMENT OPTIONS: STRESS URINARY INCONTINENCE & PELVIC ORGAN PROLAPSE

A. Surgical Mesh

Surgeons began using surgical mesh products in the 1950s to repair abdominal hernias. In the 1970s, gynecologists began surgically repairing prolapsed organs with surgical mesh products designed for abdominal hernia repairs. In the 1990s, gynecologists began using this mesh for the surgical treatment of pelvic organ prolapse ("POP") and stress urinary incontinence ("SUI"). Then, BSC, along with other manufacturers, modified hernia mesh products into products specifically intended to treat POP, SUI, or both. Today, BSC sells pelvic mesh products that include not only surgical mesh, but also insertion tools and tissue fixation anchors.

In 2002, BSC began selling Advantage Mesh for treatment of SUI resulting from urethral hypermobility and / or intrinsic sphincter deficiency and to reinforce soft tissue where weakness exists in the urological, gynecological, or gastroenterological anatomy. Advantage Mesh consists of a knitted polypropylene monofilament fiber mesh. BSC used Advantage Mesh in these six (6) sling products:

1) Advantage Transvaginal Mid-Utheral Sling System;
2) Advantage Fit System;
3) Lynx Subpubic Mid-Urethral Sling System;
4) Obtryx (including Obtryx II) Transobturator Mid-Urethral Sling System;
5) Prefyx PPS System; and

6) Solyx SIS System.

These sling products included the same Advantage Mesh, despite offering surgeons different placement routes and techniques.

In 2005, BSC began marketing Polyform Synthetic Mesh ("Polyform"). Polyform is a non-absorbable synthetic mesh, constructed of knitted filaments of polypropylene. BSC marketed Polyform to surgeons for tissue reinforcement and stabilization of fascial structures of the pelvic floor in vaginal wall prolapse, where surgical treatment is intended, either as mechanical support or bridging material for the fascial defect. BSC sold Polyform as a stand-alone polypropylene mesh and previously sold Polyform as a component in two of BSC's POP kits:[2]

1) Pinnacle Pelvic Floor Repair Kit (Anterior/Apical, Posterior, Duet); and

2) Uphold Vaginal Support System/Arise Apical Anterior Vaginal Support System.

Both POP kits used the same monofilament, macroporous, polypropylene mesh. As a stand-alone product, BSC provided Polyform in sheet form to be cut to size and sutured by the surgeon.

B. Stress Urinary Incontinence[3]

Approximately one of three women over the age of 45 years old has some form of urinary incontinence. The majority of those women do not seek medical advice or treatment for a variety of reasons.

In a continent individual, increased abdominal pressure is evenly distributed over the bladder, bladder neck, and urethra. The urethral sphincter is thus able to withstand this pressure and maintain continence. In a person with pure stress urinary incontinence (SUI), either the urethra is hypermobile or the sphincter is intrinsically deficient. In urethral hypermobility, the urethrovesical junction (UVJ) is displaced extra-abdominally, and the increased intra-abdominal pressure is unevenly distributed such that the sphincter can no longer withstand the pressure and urine leaks. With intrinsic sphincter deficiency (ISD), the UVJ is not hypermobile; however, the

[2] Connor Dep. (Vol. 4) 387:4-8.

[3] For this section, *see generally* FDA.gov (2013) Stress Urinary Incontinence, WebMD.com (2013), Mechanical Devices for Urinary Incontinence in Women, Netdoctor.com (2013) Stress Urinary Incontinence Pelvic Floor Exercises, Emedicine-Medscape.com (2013) Burch Colposuspension and Womensdoctor.com (2013), Burch Procedure and Paravaginal Repair, Emedicine-Medscape.com (2013) Vaginal Sling Procedures and Womensdoctor.com (2013) Burch Procedure and Paravaginal Repair, Wikipedia.org (2013) Urinary Incontinence.

maximal urethral closing pressure, the Valsalva leak-point pressure, or both are too low to withstand the increase in intra-abdominal pressure and, thus, urine leaks past the sphincter.

SUI is the involuntary leakage of urine during moments of physical activity that increases abdominal pressure, such as coughing, sneezing, laughing, or exercise, in the absence of a bladder contraction. It has been estimated that 14% of women have SUI. SUI is a common type of urinary incontinence in women. Urodynamic proven SUI is found in approximately 50% of women presenting for evaluation of urinary incontinence. Symptomatic women with SUI have social or hygienic consequence from their urine loss. SUI can happen when pelvic tissues and muscles, which support the bladder and urethra, become weak and allow the bladder "neck" (where the bladder and urethra intersect) to descend during bursts of physical activity (urethral hypermobility). This descent can prevent the urethra from working properly to control the flow of urine. SUI can also occur when the sphincter muscle that controls the urethra weakens (intrinsic sphincter deficiency). The weakened sphincter muscle is not able to stop the flow of urine under normal circumstances, and when there is an increase in abdominal pressure. Weakness may occur from pregnancy, childbirth, aging, or prior pelvic surgery. It has been estimated that a majority of incontinent women have a combination of urethral hypermobility and ISD. Other risk factors for SUI include chronic coughing or straining, constipation, obesity and smoking. Finally occult or latent SUI is defined as a positive stress test, loss of urine with increased intra-abdominal pressure and between 350-450cc volume in the bladder, after the repositioning of pelvic organ prolapse (usually accomplished with a ring pessary carefully positioned as to avoid compression of the urethra) in an otherwise clinically continent patient.

1. *Nonsurgical Treatment of SUI*[4]

There are numerous non-surgical treatments available to woman with SUI. First, pelvic floor exercises: a type of exercise to strengthen the pelvic floor by contracting and relaxing the levator muscles that surround the opening of the urethra, vagina, and rectum. These exercises, commonly referred to as Kegel exercises, improve the pelvic floor muscles' strength and function. Kegel exercises can improve over-active bladders by increasing urethral resistance with can trigger the bladder to relax.

[4] For this section, *see* WebMD.com (2013) Mechanical Devices for Urinary Incontinence in Women and Netdoctor.com (2013) Stress Urinary Incontinence Pelvic Floor Exercises.

Second, pessary: a removable device that is inserted into the vagina against the vaginal wall and urethra to support the bladder neck. This helps reposition the urethra to reduce SUI. These can be made of rubber, latex or silicone. Inserted into the vagina, a pessary rests against the back of the pubic bone and supports the bladder. Pessaries are available in various forms, including donut and cube shapes, and must be fitted by a healthcare provider. Some women who have stress incontinence use a pessary just during activities that are likely to cause urine leakage, such as jogging. Special incontinence pessaries have a 'knob', which fits under the urethra to elevate the midurethra to prevent urine loss.

Third, transurethral bulking agents: bulking agent injections are applied around the urethra that make the space around the urethra thicker, thus helping to control urine leakage. The effects are usually not permanent.

Fourth, behavioral modification: this includes avoiding activities that trigger episodes of leaking. Lifestyle modification can improve stress incontinence symptoms and include quitting smoking, weight loss and allergy treatment during seasonal allergies.

Fifth, urinary seals: these are adhesive foam pads, which women place over the urethral opening. The pad creates a seal and prevents the leakage of urine, providing incontinence treatment. The pad is removed before urination and replaced with a new one afterward. The pad can be worn during exercise or physical activity but not during sexual intercourse.

Sixth, urethral insert: a thin, flexible tube that is solid rather than hollow (like a catheter) is placed into the urethra to block the leakage of urine These small plugs are inserted into the urethra by women to prevent leakage and are removed prior to urination. These inserts can be uncomfortable and may increase the risk of urinary tract infection.

Seventh, bladder neck support device: this device is a flexible ring with two ridges. Once inserted into the vagina, the ridges press against the vaginal walls and support the urethra. By lifting the bladder neck, it provides better bladder control in women suffering from stress incontinence. The device needs to be sized to fit and must be removed and cleaned after urination. Bladder neck support devices can be uncomfortable and may cause urinary tract infections.

2. *Surgical Treatment of SUI*

a. *The Burch Culposuspension*[5]

Retropubic approaches for the treatment of stress urinary incontinence include the Burch retropubic urethropexy (both open and laparoscopic) and the Marshall-Marchetti-Krantz (MMK) procedure. The goal of both of these procedures is to suspend and stabilize the urethra so that the urethrovesical junction (UVJ) and proximal urethra are replaced intra-abdominally and to recreate a firm backstop for intra-abdominal pressure. This anatomic placement allows normal pressure transmission during periods of increased intra-abdominal pressure restoring continence in a previously incontinent, hypermobile UVJ.

The Burch procedure was described in 1961. Initially, Burch described attaching the paravaginal fascia to the arcus tendineus. However, this was later changed to Cooper's ligaments because these were felt to provide more secure fixation points, and less chance of infection as seen with the prior MMK procedure.

Patients with type III stress urinary incontinence (a fixed, nonfunctioning proximal urethra) are not ideal candidates for a Burch procedure as no hypermobility exists to correct. For the Burch procedure, a low Pfannestiel incision is made above the pubic bone in order to enter the space of Retzius (the anatomical space between the pubic bone and the bladder above the peritonium in order to suspend the bladder and/or to perform a paravaginal repair. The procedure involves placing permanent stitches adjacent to the neck of the bladder and either proximal or distal to the bladder neck stitches on each side and suturing them Cooper's ligament which is attached to the pubic bone. The paravaginal repair is very similar except that the stitches are attached to the arcus tendentious linea pelvis. The likelihood of success of the Burch and the paravaginal repair procedures is reported to be 80-90% in most cases. Success means total elimination of the incontinence and patient satisfaction score greater than 90%. Improved means significant reduction of urine loss and greater than 70% improvement of patient satisfaction scores. Additionally, these retropubic procedures can be accomplished by the laparoscopic route. With respect to the selection of synthetic absorbable suture versus non-absorbable suture, and braided versus monofilament, no prospective randomized blinded data exist to suggest superiority of one suture material over another. However, recognized risks are associated with bone anchors.

[5] For this section, *see* Emedicine-Medscape.com (2013) Burch Colposuspension and Womensdoctor.com (2013) Burch Procedure and Paravaginal Repair.

Modifications in the technique can be used if co-existent central defect cystocele is present and obliteration of the cul-de-sac can be performed to prevent enterocele or posterior vaginal wall prolapse after Burch colposuspension.

b. *Pubovaginal sling procedures*[6]

Pubovaginal slings have excellent overall success and durable cure. The procedure involves placing a band of autologous, allograft, xenograft or synthetic material directly under the bladder neck (i.e., proximal urethra) or mid-urethra, which acts as a physical support to prevent bladder neck and urethral descent during physical activity. This is brought up through the rectus fascia. The sling also may augment the resting urethral closure pressure with increases in intra-abdominal pressure.

Historically, surgeons have used the fascia lata sling for recurrent SUI after a failed anti-incontinence operation. Furthermore, this operation is used extensively for the treatment of primary ISD. If the abdominal tissues are weak and attenuated or if the vaginal tissues are atrophied or in short supply, constructing a pubovaginal sling from the leg fascia lata can be performed. This procedure is more involved than the creation of the rectus fascial sling as it requires a second incision to harvest the fascia lata and healing in an area remote for the index procedure.

An alternative to a long rectus sling is construction of a short sling from a much smaller piece of abdominal fascia (rectus fascia suburethral sling). The surgical procedure is similar to that used for the rectus fascia pubovaginal sling, except that the harvested fascial tissue is much smaller and the operation time shorter. The advantage of this procedure is its simplicity. No extensive dissection in the suprapubic area is necessary, and the postoperative result is similar to that of the full-length fascial strip sling.

An alternative to a long fascia lata sling is the use of a postage stamp–sized patch of fascia lata from the outer thigh (fascia lata suburethral sling). The surgical procedure is similar to that for the fascia lata pubovaginal sling, except the harvested fascia is much smaller. This operation does not require extensive dissection in the thigh area, and the postoperative result is similar to that of the full-length fascia lata strip sling. Postoperative convalescence is shorter than that of the fascia lata pubovaginal sling procedure.

[6] For this section, *see* Emedicine-Medscape.com (2013) Vaginal Sling Procedures and Womensdoctor.com (2013) Burch Procedure and Paravaginal Repair.

The vaginal wall suburethral sling helps restore urethral resistance by increasing urethral compression and improving mucosal coaptation of the bladder neck. This operation is attractive because it is simple and easy to perform. Postoperative complications are minimal, and the recuperative period is short. Vaginal sling surgery is relatively contraindicated in elderly women with atrophic vaginitis. If recognized before surgery, the atrophied vaginal wall may be revitalized with the administration of vaginal estrogen cream or tablets for 3-6 months.

A clear contraindication to pubovaginal sling surgery is pure urge incontinence or mixed urinary incontinence (MUI) in which urge is the predominant component. An inherent risk of any sling procedure is de novo or worsening urge symptoms; thus, surgeons must identify and treat the presence of an urge component before surgery.

Conversely, poor detrusor function is a relative contraindication to pubovaginal sling surgery because the potential for urinary retention is increased. Women with absent or poor detrusor function in the presence of SUI are at a higher risk of experiencing prolonged postoperative urinary retention.

c. *Mid-Urethral Synthetic Slings*

Based on the "Integral theory of female incontinence," Professor Ulmsten developed a mid-urethral procedure with synthetic material to treat SUI. The first reports of this procedure appeared in 1996 as an intravaginal slingoplasty. The "tape'" was place through a small vaginal incision at the midurethra, brought through the urogenital diaphragm through the retropubic space and exited through small suprapubic incisions. The operation was theorized to correct incontinence by recreating the mid-urethral support of the pubourethral ligament and also by creating a mid-urethral hammock for support of the urethra during stress events. The procedure was described to have a success rate of 85-90% with an additional 5-10% significantly improved. The Gynecare TVT system was introduced in the US in November of 1998. Early studies showed that the risk of bladder perforation during the procedure occurred 5-10% of cases and vascular injury with without hematoma formation occurred in 2-5% of patients.

In an attempt to decrease the risk of bladder perforation and vascular injury, a "top-down" approach to trocar placement was promoted as the SPARC procedure, introduced in the US in 2001 by American Medical Systems (AMS). The next modification of the mid-urethral sling came in 2001 when Delorme described his results for the use of the obturator membrane and inner thigh for passage of the sling material. The proposed advantage was avoidance of the retropubic space,

thus avoiding bladder perforation and retropubic vascular injury. The trocars were passed from the inner thigh through the obturator membrane from an "outside – in direction".

The next modification came from de Leval in 2003, with the "inside-out" trocar placement for the transobturator sling. The final modification came around 2006 with the release of the mini-slings, or single incision slings, which use support devices at the ends of shorter mesh lengths to accomplish fixation without the need for a secondary cutaneous exit point. The mini-slings could be placed in a retropubic or "U" fashion or a hammock or "H" fashion.

3. *Boston Scientific's Advantage, Advantage Fit, and Lynx*

The Advantage and Advantage Fit Transvaginal Mid-Urethral Tension-Free Sling Systems are mid-urethral slings that are designed by Boston Scientific to support the urethra at its midpoint without sutures, in the rectus Fascia. The sling is comprised of a polypropylene mesh; the suburethral portion (approximately 4 centimeters) is "detanged" meaning the edges of the mesh have been heat sealed. The Advantage Transvaginal Sling System includes the delivery device (a 5mm curved needle or trocar); a dilator tube / mesh assembly; and the mesh.[7] The Advantage and Advantage Fit Transvaginal Mid-Urethral Tension-Free Sling Systems are designed to be inserted through the retropubic space through the top-down approach. The main difference of the Advantage Fit (introduced in 2008) is the diameter of the trocar (2.7 mm vs. 5 mm) and the degree of curvature of the trocar (17% tighter curve) which places the mesh closer to the pubic bone.

The Lynx Suprapubic Mid-Urethral Sling System is a tension-free sling system intended for the treatment of SUI resulting from urethral hypermobility and /or Intrinsic Sphincter Deficiency. BSC introduced the Lynx in 2004. It is a sterile, single-use system, consisting of two delivery devices and one mesh assembly. The mesh assembly is comprised of a polypropylene knitted mesh protected by a disposable plastic sleeve. The disposable delivery device consists of a handle with a curved needle. The longer needle is designed to facilitate the passage of the mesh assembly through challenging tissues for suprapubic placement.[8]

4. *Boston Scientific's Obtryx & Prefyx*

The Obtryx Transobturator Mid-Urethral Sling System ("Obtryx") and Prefyx PPS™ System ("Prefyx") are intended for use as suburethral slings for the treatment of stress urinary incontinence resulting from hypermobility, intrinsic sphincter deficiency, or both. The mesh

[7] BSCM06300021197.
[8] *Id.*

implants marketed as Advantage, Advantage Fit, and Lynx are identical to the mesh implants marketed as the Obtryx (introduced in 2004) and Prefyx. The Obtryx and Prefyx offer different surgical delivery placement routes for the mesh implants: transobturator (Obtryx) and pre-pubic (Prefyx). The two additional delivery placement routes also deliver the mesh to the suburethral area but do so through the transobturator route (Obtryx) or prepubically (Prefyx). With the Obtryx, surgeons place the mesh implants through the obturator foramen / muscle / membrane behind the pubic bone (percutaneous), exiting the vaginal vault. With the Prefyx (introduced in 2007), surgeons place the mesh implants in front of the pubic bone (transvaginal) until exiting the body approximately 1-2 cm below the pubic tubercles. For both, BSC developed delivery devices to place the surgical mesh sling using the prepubic or transobturator delivery placement route.

Unlike all other BSC Mesh Products, BSC gathered clinical data on the safety and effectiveness of the Prefyx prior to launch. The study evaluated subjects three months after Prefyx placement and found a failure rate of 15.1%.[9] Through this study, BSC also observed the following adverse events within only three months of Prefyx placement:

- recurrent SUI: 9 (9.7%);
- post-operative pain (resolved within 10 days after narcotics medications): 6 (6.5%);
- fever (within 10 days of procedure): 6 (6.5%);
- *de novo* dyspareunia (resolved by 3 months): 4 (4.3%);
- transient urinary retention: 3 (3.2%);
- exposure / erosion: 2 (2.2%);
- foreign body reaction requiring removal (by week 1): 1 (1.1%); and
- intraoperative vaginal wall perforation: 1 (1.1%).[10]

In contrast to these results, the authors concluded, "pre-pubic sling placement is a relatively safe and effective alternative to traditional retropubic and transobturator approaches."[11]

BSC also collected data one year after Prefyx placement and recorded the results in a final study synopsis. At one year, BSC observed serious adverse events in 12% of patients implanted with a Prefyx. In addition, BSC found device-related adverse events in 73% of patients. BSC detected post-procedural pain (29%) and stress incontinence (15%) as the device-related adverse

[9] BSCM05300048255, at -258.
[10] *Id.* at -258-59.
[11] *Id.*

events with the highest incidence.[12] At one year, the study determined the Prefyx cured incontinence in 81.7% of patients.[13] BSC discontinued the Prefyx in 2012.

5. *Boston Scientific's Solyx*

The Solyx™ SIS System ("Solyx") is intended for use as a suburethral sling for the treatment of SUI resulting from urethral hypermobility and / or intrinsic sphincter deficiency. Unlike BSC's previously discussed slings, placement of the Solyx (introduced December 2008) requires a single incision through the vaginal wall at the level of the mid-urethra. The loaded delivery device is inserted through the vaginal wall incision and guided to the proper deployment site in the obturator internus muscle, of the anchor which is attached to the mesh, on one side of the body. The Solyx is 9 cm in length. Upon delivery of the mesh assembly to the proper locale, the carrier is disengaged from the delivery device, the delivery device is removed back through the vaginal incision, and the process is repeated on the contralateral side.

C. Pelvic Organ Prolapse

POP occurs when the tissue and muscles of the pelvic floor no longer support the pelvic organs resulting in the drop (prolapse) of the pelvic organs from their normal position. The pelvic organs include the vagina, cervix, uterus, bladder, urethra, and rectum. Thirty to fifty percent of women may experience POP in their lifetime with 2 percent developing symptoms. When POP occurs, the organs bulge (prolapse) into the vagina and sometimes prolapse past the vaginal opening. More than one pelvic organ can prolapse at the same time. Organs that can be involved in POP include the bladder, the uterus, the rectum, the top of the vagina (vaginal apex) after a hysterectomy, and the bowel. The bladder is the most commonly involved organ in pelvic organ prolapse.

POP is often brought about when the supporting muscles and tissue of the pelvic floor become torn or stretched because of labor or childbirth or may weaken with age. Other risk factors for POP include: genetic predisposition, connective tissue disorder, obesity and frequent constipation. Many women have some degree of POP, although not all women have symptoms. POP can affect the quality of life (QOL) of women, however POP is not a life-threatening condition. Symptoms of POP are usually limited to QOL issues such as the sensation of pelvic fullness, pressure, interference with satisfactory sexual activity, as well as possibly altering normal

[12] BSCM04800061797, at -802-04.
[13] *Id.* at -803.

urination and bowel function. The most characteristic symptom of POP is a sensation of bulging or fullness in the vagina that worsens throughout the day. POP is a common condition with up to 50% of women who have had children having some degree of POP.

1. *Treatment For POP*

POP is a problem of increasing frequency and prevalence as women age. United States Census Bureau predicts that the percentage of women in the US greater than 45 years old will continue to increase. This ever increasing segment of population and potential surgical market creates a desirable target for device manufactures eager to capture a market share for devices used in the treatment of incontinence and pelvic organ prolapse. Nonsurgical or surgical treatments options are available to patients with POP. Some nonsurgical treatment options, in addition to medication, for POP include:

- Pelvic Floor Exercises: A type of exercise to strengthen the pelvic floor by contracting and relaxing the muscles that surround the opening of the urethra, vagina, and rectum. The exercises are commonly referred to as Kegels; and

- Pessary: A removable device that is inserted into the vagina to support the pelvic organ(s) that have prolapsed.

Not every woman with POP will need surgery. If surgery is recommended, factors to consider include: which organ(s) have prolapsed, severity of prolapse, desire for future children, age, sexual activity, and severity of symptoms. Surgery to repair POP can be done through either the vagina or abdomen, using stitches (sutures) alone as done with traditional POP surgery or with the addition of surgical mesh manufactured by medical device companies. Surgical options include restoring the normal position of the vagina, repairing the tissue around the vagina, permanently closing the vaginal canal with or without removing the uterus (colpocleiesis). It is also possible that women with POP may experience problems with urine leakage (incontinence). During surgery, a procedure to prevent or decrease urine leakage may be performed. In the United States alone, approximately 200,000 women will elect to undergo a surgical procedure for POP.

Traditional POP surgery is performed from either the vagina (termed “transvaginal”) or from the abdomen (termed “transabdominal), with the latter group being performed either with an abdominal incision (Abdominal Sacrocolpopexy) or with minimally invasive procedures such as with laparoscopic or robotic technology.

Traditional surgery, also known as native tissue repair with suture, is performed without a synthetic mesh to hold up the prolapsing pelvic organ. Traditional surgery uses only sutures placed into the native tissues surrounding the prolapsing portion of the vagina to repair the POP. In general, there are several differences between traditional, transvaginal non-mesh and transvaginal mesh kit POP surgeries:

- No synthetic, non-absorbable meshes are used in traditional POP surgery;
- No trocars/guides are used to place the mesh into position in traditional POP surgery;
- There is no tensioning of mesh arms with traditional surgery;
- The traditional procedure is performed under direct vision, meaning that the surgeon can see what he/she is doing with no blind passing of trocars/needles.

The use of transvaginal synthetic mesh for POP repair was marketed mainly as claiming to increase the durability of the POP repair relative to traditional, non-mesh transvaginal POP surgery. However, starting in 2008, the FDA issued a Public Health Notification and subsequent safety information on the serious complications associated with surgical mesh placed through the vagina to treat POP. Based on an updated analysis of adverse events reported to the FDA and complications described in the scientific literature, the FDA identified surgical mesh for transvaginal repair of POP as an area of continuing serious concern. The FDA declared the serious complications from transvaginal mesh were "not rare" (emphasis in original). The FDA also concluded "it is not clear that transvaginal POP repair with mesh is more effective than traditional non-mesh repair in all patients with POP and it may expose patients to greater risk." From 2008 – 2010, the most frequent complications reported to the FDA for surgical mesh devices for POP repair included mesh erosion through the vagina, pain, infection, bleeding, pain during sexual intercourse (dyspareunia), organ perforation, and urinary problems. There were also reports of recurrent prolapse, neuro-muscular problems, vaginal scarring/shrinkage, and emotional problems. Many of these complications require additional intervention, including medical or surgical treatment and hospitalization. The FDA's systematic review of the relevant scientific literature revealed: mesh used in transvaginal POP repair introduces risks not present in traditional non-mesh surgery for POP repair and mesh placed abdominally for POP repair appears to result in lower rates of mesh complications compared to transvaginal POP surgery with mesh.

2. *Boston Scientific's Pinnacle and Uphold*

BSC designed the Pinnacle® Anterior-Apical, Pinnacle® Posterior Repair Kit, and Pinnacle® Duet Repair Kit Systems (collectively, "Pinnacle") for repair of anterior, apical, and posterior vaginal wall defects in a single patient. BSC constructed the Pinnacle (introduced in 2007) with its Polyform product, a non-absorbable polypropylene mesh. Each Pinnacle kit contained Polyform mesh cut into specific shapes and sizes to match three (3) anatomical POP defects: (1) anterior defects; (2) apical defects; and (3) posterior defects. BSC configured all three Pinnacle devices with two mesh legs for placement through the sacrospinous ligament for apical vaginal wall support. BSC also designed the Anterior-Apical and Duet Kits with two additional legs for placement through the arcus tendinous for anterior vaginal wall support. In the Anterior-Apical configuration, BSC provided a single mesh assembly intended for total repair, anterior repair only, or apical repair only. In addition to total repair, the Anterior-Apical configuration allowed surgeons to cut off pieces of the Pinnacle to perform anterior or apical repairs only. The Duet Kit provides two separate functional pieces in a single package for the convenience of the surgeon for the repair of both anterior and posterior defects. BSC provided surgeons a Capio device with all three Pinnacle devices to deliver the mesh through the patient's pelvic floor to the desired anatomy.

The Pinnacle Pelvic Floor Repair Kit II, marketed as Uphold™ Vaginal Support System ("Uphold"), was indicated for tissue reinforcement and stabilization of fascial structures of the pelvic floor for vaginal wall prolapse, as mechanical support or bridging material for the fascial defect. BSC constructed the Uphold (introduced in 2008) with its Polyform product, a non-absorbable polypropylene mesh. The Uphold offered an intra-vaginal approach for a specific POP repair, designed to provide support at the vaginal apex and additional support to prevent concomitant anterior prolapse in the future. Indicated for repairs of the vaginal apex only, BSC designed the Uphold with "approximately 75 percent less mesh than a total mesh lift kit."[14] While BSC configured the Pinnacle Anterior-Apical and Duet Kit with four legs to attach to the sacrospinous ligament and pelvic side walls for support, the Uphold only uses the two legs that attach to the sacrospinous ligament for support.

[14] Dep. of Roger Goldberg 368:23-369:8.

BSC withdrew the four (4) Uphold and Pinnacle devices from the marketplace on January 31, 2013.

IV. OPINIONS

A. BSC Constructed The Mesh Products With Polypropylene That Is Not Suitable In A Permanent Transvaginal Implant.

1. *Polypropylene Can Degrade in a Woman's Vagina and Pelvis.*

The placement of permanent polypropylene mesh in the human vagina creates problems because of the chemical composition and structure of the mesh and the physiological conditions of the vagina and the surrounding tissues. The field of urogynecology in medicine has been forced to confront and study the material properties of polypropylene mesh to understand the etiology of the complications we treat as physicians. The etiological study of mesh complications has required the field or urogynecology to scientifically analyze the role of the products in treated or untreated women with the medical condition. Much literature related to the material properties of polypropylene mesh, its material characteristics, and the effects on it in vivo comes from medical literature in the fields of general surgery and subspeciality of urology or urogynecology. However, physicians that treat women with mesh complications also review peer reviewed articles on biomaterials as further basis for the scientific understanding of polypropylene mesh performance. Numerous studies over the last 30 years show polypropylene as chemically reactive and not inert, with flaking and fissuring demonstrated by scanning electron microscopy, which leads to degradation. Polypropylene contains compounds toxic to human tissue that leach out when degradation occurs in the human pelvis, enhancing the intensity of fibrosis and the body's inflammatory reaction.[15] The enhanced inflammatory and fibrotic reactions within the tissues in the pelvic floor cause a multitude of problems.[16] There have been recent studies suggesting that oxidation of the mesh occurs because of the polypropylene and the conditions in which it is placed.[17] The oxidation causes the mesh to degrade, crack and break apart.[18] In another recent study, *Clave et al*. compared 100 pelvic mesh implants and found evidence of degradation in every

[15] Sternschuss et al., *Post-Implantation Alterations of Polypropylene in the Human*, 188 J. UROL. 27 (2012).

[16] Coda A, Hernia 2003;7:29; Jongebloed, WL, *Degradation of Polypropylene in the Human Eye: A SEM Study*, 64 DOC. OPHTHALMOL. 143-152 (1986); Skrypunch, OW, *Giant Papillary Conjunctivitis from an Exposed Prolene Suture*, 21:5 Can. J. Ophthalmol. 189-92 (1986).

[17] Costello et al., *Characterization of Heavyweight and Lightweight Polypropylene Prosthetic Mesh Explants from a Single Patient*, 14 SURGICAL INNOVATION 168-176 (2007).

[18] *Id.*

explanted material after only three months in vivo. In addition, infection or inflammation enhanced degradation. The authors in that study concluded polypropylene is indeed not inert.[19]

Because of the structural complexities and nature of the chemicals ordinarily found in the vagina and its surrounding tissues, polypropylene presents unique problems when placed in the vagina for several reasons. A 2011 Engineering Bulletin from Propex, entitled "EB-405, The Durability of Polypropylene Geotextiles for Waste Containment Application," states, "polypropylene is vulnerable to the following substances: highly oxidized substances such as (peroxide), certain chlorinated hydrocarbons (halogenated hydrocarbons), and certain aromatic hydrocarbons."[20] Vaginal and perivaginal tissues are ready sources for peroxide. The vaginal species lactobacillus produces hydrogen peroxide and lactic acid from glycogen that is produced in the squamous cells of the vagina. Estrogen catalyzes the production of glycogen from the vaginal cells. The hydrogen peroxide produced from the lactobacillus species plays an important role in controlling the vaginal micro-flora. In fact, the vagina is a ready source of hydrogen peroxide production. In a manuscript from M Strus, "The In Vitro Effects of Hydrogen Peroxide on Vaginal Microbial Communities," the authors show the amount of hydrogen peroxide produced by the lactobacillus species.[21] "Hydrogen Peroxide reached concentrations of from 0.05 to 1.0 mM, which under intensive aeration increases even up to 1.8 mM."[22] These results confirmed the previous results of M Strus.[23]

Aromatic hydrocarbons can be found in the human body. In a paper from HB Moon entitled, these aromatic hydrocarbons were noted to be present in, "[t]otal concentrations of PAHs and SMCs in adipose tissues rang[ing] from 15 to 361 (mean:119) ngg(-1) lipid weight and from 38 to 253 (mean:106) nng(-1) lipid weight respectively . . . . The results of this study provide baseline information on exposure of PAHs and SMCs to the general population in Koreans."[24]

It has also been determined that halogenated hydrocarbons can be found not only in adipose tissue but also the blood stream. A 1979 publication found halogenated hydrocarbons, pesticide

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[19] *See* Clave et. al, *Polypropylene As A Reinforcement In Pelvic Surgery Is Not Inert: Comparative Analysis of 100 Explants*, 21 INT. UROGYNECOL. J. 261-70 (2010).

[20] Citing Schneider, *Long Term Performance of Polypropylene Geosynthetics. Durability and Aging of Geosynthetics*, 95-109 (Elsevier 1989).

[21] Strus et al., *The In Vitro Effect of Hydrogen Peroxide in Vaginal Microbial Communities*, 48:1 FEMS IMMUNOL. MED. MICROBIOL. 56-63 (2006).

[22] *Id.*

[23] Strus et al., *Hydrogen Peroxide Produced by Lactobacillus Species as a Regulatory Molecule for Vaginal Micro-flora*, 56 MED. DOSW. MIKROBIOL. 1:67-77 (2004).

[24] Moon, *Occurrence and Accumulation Patterns of Polycyclic Aromatic Hydrocarbons and Synthetic Musk Compounds in Adipose Tissues of Korean Females*, 86 CHEMOSPHERE 485-90 (2012).

by-products, both in human adipose tissues and the blood stream.[25] In a subsequent paper from 1985 in *Environmental Health Perspectives*, Henry Anderson also found these pesticide by-products in human adipose tissue.[26] Accordingly, the body location where the polypropylene mesh is being placed can expose it to known chemical degradation agents.

However, chemical degradation is not the only way that polypropylene degrades in vivo. In a 2011 paper from Das, the researchers found found that various bacteria such as Pseudomonas species, Bacillus species, Mycobacterium and Corynebacterium species, which are present in a woman's vagina, can degrade petroleum hydrocarbons. Also fungi such as the Candida species, also present, can degrade petroleum-based hydrocarbons.[27]

Microbial agents that can be found inside the normal and abnormal flora of the human vagina such as Candida and, with certain pelvic infections such as Bacillus and Pseudomonas, can be a source of biological degradation of polypropylene products. Polypropylene degradation products and residues can form carbon monoxide, acrolein, aldehydes and acids, qualifying these health hazards as toxic and irritants.[28] A 2011 paper from the University of Gothenburg explains, "[n]on-biodegradable polymers can be degraded by heat, oxidation, light, ionic radiation, hydrolysis and mechanical shear, and by pollutants such as carbon monoxide, sulphur dioxide, nitrogen oxide and ozone. This causes the polymer to get brittle, to fragment into small pieces and to release degradation products."[29] Lithner continues, "[o]ther substances (besides monomers) are often needed for polymerization to occur, for instance initiators, catalysts, and, depending on manufacturing process, solvents may also be used. The resulting plastic polymer can be blended with different additives, for instance plasticizers, flame retardants, heat stabilizers, antioxidants, light stabilizers, lubricants, acid scavengers, antimicrobial agents, anti-static agents, pigments, blowing agents and fillers, and is finally processed into a plastic product. There are many different plastic polymers and several thousand different additives, which result in an extremely large

[25] Peoples et al., *Determination of Volatile Purgeable Halogenated Hydrocarbon in Human Adipose Tissue and Blood Stream*, 23:1 BULLETIN ENV. CONTAM. & TOX. 244-49 (1979).

[26] Anderson, *Utilization of Adipose Tissue Biopsy and Characterizing Human Halogenated Hydrocarbon Exposure*, 60 *Env. Health Persp.* 127-31 (1985)

[27] Das et al., *Review Article: Microbial Degradation of Petroleum Hydrocarbon Contaminants: an Overview*, 941810 J. Biotech. Res. Int'l 1-13 (2011).

[28] *Health, Safety and Environment Fact Sheet: Hazardous Substances - Plastics*, from CAW/TCA (www.caw.ca), (2011):343,

[29] Lithner et al., *Environmental and Health Hazards of Chemicals in Plastic Polymers and Products*, at 4 (2011) (citations omitted).

variation in chemical composition of plastic products."[30] "Since plastic products are composed of many different chemicals, and the main part of these [are] broken down into something completely different; this complicates the prediction."[31] "The type and quantity of degradation products formed may also be influenced by degradation mechanisms, presence of polymerization impurities, and surrounding factors, e.g. temperature and oxygen."[32] "Few studies combining leaching tests with toxicity tests have been performed on plastic products."[33]

The available peer-reviewed literature regarding degradation/oxidation of polypropylene in the human body dates back to the 1960's and has been reported in numerous such publications.[34] Two of the more important and salient articles regarding reported degradation in explanted surgical meshes (hernia and pelvic floor) are the *Costello* and *Clave* articles.

In his paper, "Characterization of Heavyweight and Lightweight Polypropylene Prosthetic Implants from a Single Patient," Professor Costello reported that hernia mesh made of polypropylene oxidized and degraded as a result of the metabolites produced by phagocytic cells during the body's inflammatory reaction to the mesh. High-magnification photographs showed cracking and peeling of the polypropylene fibers.

In the *Clave* article, "Polypropylene as a Reinforcement in Pelvic Surgery is Not Inert: Comparative Analysis of 100 Explants," also displayed high magnification photos of polypropylene fibers from explanted meshes and, in this case, the meshes were explanted from women's pelvic floor tissues.[35] The heavyweight meshes showed even greater cracking than the lower density meshes, but according to Professor Clave, all 84 of the polypropylene explants examined showed degradation. As a potential cause for the oxidative degradation of the mesh within the "septic environment," the article identifies the free radical attack through the synthesis of peroxides, superoxides, and hypochlorous acid during the chronic inflammatory phase.[36]

Given the information available to BSC in the scientific and medical literature concerning the potential for degradation of polypropylene, it is my opinion to a reasonable degree of medical

[30] *Id.* at 6 (citations omitted).
[31] *Id.* at 8.
[32] *Id.* at 9.
[33] *Id.* at 12.
[34] Liebert et al., *Subcutaneous Implants of Polypropylene Filaments*, 10 J. BIOMED. MATER. RES. 939-51 (1976); Williams, *Review of Biodegradation of Surgical Polymers*, 17 J. Materials Sci. 1233-46 (1982); Oswald et al., *The Deterioration of Polypropylene By Oxidative Degradation*, 5 POLYMER ENG. SCI. 152-58 (1965).
[35] Clave (2010).
[36] *Id.*

certainty that a reasonably prudent medical device manufacturer such as BSC could have conducted clinically relevant testing to determine if naturally occurring conditions in the vagina could cause polypropylene to degrade and if so, what the quantity and quality of the products of degradation would be, whether they would be released into surrounding tissues and/or migrate in the woman's body, what the clinical implications for the woman would be and whether some women's bodies react differently to the mesh and the degradative process and its by-products.

It further is my opinion to a reasonable degree of medical certainty that the mesh in the BSC Mesh Products degrades. The effect of chemical and biological degradation of these meshes in a woman's tissues can lead to a greater foreign body reaction, enhanced inflammatory response and excessive scarring, which can lead to severe complications in patients, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, chronic dyspareunia, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, bladder and urethra, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others. As a result, the polypropylene in BSC Mesh Products' meshes is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women.

2. *The Polypropylene Used in BSC's Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Prefyx, Pinnacle and Uphold Products Was Never Meant to be Used in the Human Body*

Chevron Phillips Chemical Company ("CPCC") Marlex Polypropylene resin was used by BSC to manufacture the polypropylene mesh contained in the BSC Mesh Products, as well as many other polypropylene meshes manufactured by BSC.[37] According to Chevron Phillips and its material safety data sheets, this polypropylene resin should never have been used for human medical device implant applications. In 2004, CPCC first added the following Medical Application Caution ("MAC") to the MSDS for Marlex (polypropylene):[38]

> MEDICAL APPLICATION CAUTION: Do not use this Chevron Phillips Chemical Company LP material in medical applications involving permanent implantation in the human body or permanent contact with internal body fluids or tissues.

[37] BSCM05100122946.
[38] BSCM04500000465.

> Do not use this Chevron Phillips material in medical applications involving brief or temporary implantation in the human body or contact with internal body fluids or tissues unless the material has been provided directly from Chevron Phillips Chemical Company LP under an agreement which expressly acknowledges the contemplated use.
>
> Chevron Phillips makes no representation, promise, express warranty, or implied warranty concerning the suitability of this material for use in implantation in the human body or in contact with internal body fluids or tissues.

CPCC also included the MAC on the 2007 version of the Marlex MSDS.[39] At this same time, the section describing reactivity was expanded to state: "**Incompatibility With Other Materials**: May react with oxygen and strong oxidizing agents, such as chlorates, nitrates, peroxides, etc." [40] A CPCC document notes the following:

- Table 2 lists several strong mineral acids, halogens and oxygen which can chemically attack Marlex polypropylene, causing degradation of the resin[41]
- If an oxidizing chemical . . . comes in contact with Marlex polypropylene, a chemical attack occurs which can degrade the resin permanently[42]
- The effect of strong oxidizing agents is an attack on the polymer chain resulting in eventual embrittlement of the resin[43]

Moreover, CPCC recognized that "fortunately . . . a period of time may be required for significant degradation to occur."[44]

Shortly after the imposition of the MAC, CPCC agreed to sell BSC one final shipment of Marlex. BSC negotiated this last buy in 2005, pursuant to a 2004 contract, and assured the Marlex suppliers it would "conduct the necessary testing to assure the product was safe for its intended use."[45] In 2011, BSC attempted to purchase Marlex once again from CPCC. Todd McCaslin wrote for BSC to CPCC.[46]

> If it is liability issue, I believe we can work with our Legal to draft appropriate language that fully protects PSPC. If it is financial (I realize our requirements are very small) we could discuss a minimum cost that would be attractive to PSPC.

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[39] BSCM11500004534; *see also* BSCM01300000541.
[40] BSCM04500000465 (emphasis in original).
[41] CP-0091.
[42] *Id.*
[43] *Id.*
[44] *Id.*
[45] Dep. of Rob Miragliuolo 83:4-8; *see also* BSCM05100122946.
[46] BSCM06700722580.

However, this time CPCC refused: "[t]hanks Todd, we are simply not interested in this business at any price which is still the basis for our past Agreement with your company."[47] Internally, BSC wrote about the interaction:

> I have had several communications with Senior Management at Phillips over the past several days. I met with Frank Zakrzewski, Dir Sales on Friday and found out that they do have 70K lbs of material that is in process of being transferred to a Compounding division. He was pleasant to deal with but said the decision would be made by his boss, who is the General Manager of Phillips Sumika Polypropylene Co. (Bob Rhodes) Bob and I discussed several times today. Unfortunately the result was that Phillips has no interest in dealing with BSC on this material at any price or with any type of indemnification. I will forward his response. [48]

On November 2, 2007, Ron Ciula at BSC received an e-mail from Jarden Materials, the company that extruded the Marlex Pellets into monofilament fibers concerning the MAC. Jarden announced its position to BSC on the MAC:

- It is our position that the Agreement between Boston Scientific and Phillips Sumika does not mitigate the "Medical Application Caution" statement on the Marlex MSDS. (MSDS Attached)[49]

- Or Boston Scientific must provide governmental documentation from biocompatibility studies and FDA registration indicating that the medical device and all of its subcomponents (i.e. resin) are suitable for implantation and provide Jarden with an agreement of warranty and indemnification.[50]

On November 12, 2007, BSC provided the bench testing that it had performed in 2003 and relied upon as the sole pre-market safety data.[51] On November 27, 2007, Jarden responded to BSC and indicated that the material submitted did not obviate concerns over the MAC:

> As we discussed, unfortunately Jarden Applied Material will not be able to accept purchase orders for Polypropylene monofilaments for implantable surgical mesh applications. We value our relationship with Boston Scientific and hope that we can supply your needs on other products in the future. [52]

Instead of performing additional tests or obtaining clinical data, BSC switched to a different company to extrude the monofilament fibers.[53] Similarly, BSC never received or

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[47] *Id*.
[48] BSCM04700235069.
[49] BSCM05300015468.
[50] *Id*.
[51] BSCM05300017315.
[52] BSCM05300018264.
[53] BSCM07400016872.

reviewed any information concerning testing by CPPP with respect to how the Marlex polypropylene interacts with the human body.[54] In an email dated August 3, 2011, BSC indicates its willingness to use a 3rd party to purchase the HGX-03-01 that Phillips has in inventory to avoid direct purchase— which was not possible since Phillips said that they were not interested in selling to BSC at any price.[55]

BSC also did not use medical grade polypropylene in their BSC Mesh Products. It did begin to look into medical grade polypropylene as a replacement for Marlex in 2008. In an e-mail from Proxy biomedical, BSC received quotations for a medical grade polypropylene resin project: "Provide Polypropylene Boston Scientific Mesh using a qualified spinner, knitter, and **medical grade Polypropylene resin**."[56] There are a multitude of other documents demonstrating that BSC had experience with and access to medical grade polypropylene.[57] Despite this, BSC continued (and continues to this day) to use the Marlex PP in the BSC Mesh Products.

Given the information available to BSC in the MSDS about the properties of the polypropylene, specifically about the polypropylene's incompatibility with strong oxidizing agents like peroxide, BSC should have provided this information to physicians. Because the vagina and perivaginal tissues where surgeons implant BSC's Mesh Products are ready sources of peroxide, implanted Mesh Products will undergo oxidation or degradation inside women. However, BSC never provided physicians with warnings about the Mesh Products' risk of oxidation or degradation. It is with a reasonable degree of medical certainty that the effect of chemical and biological alterations of polypropylene due to oxidation can cause the Mesh Products to either fail or undergo significant change such as shrinkage, hardening, breakage, cracking or flaking, all of which are likely to contribute to an increase in the severity and duration of inflammation in the patient implanted with a polypropylene pelvic mesh. This could also lead to products leaching out and getting absorbed into the blood stream, which could cause an immunological response. Finally, the worst case scenario would be these degradation products or these leach agents could in fact be toxic. Surgeons cannot appropriately conduct a risk-benefit analysis without knowledge of the Mesh Products' risk of oxidation or degradation. As a result of not disclosing the Mesh Products' risks of oxidation and degradation to physicians, the non-disclosure incapacitated patients from

[54] Dep. of Todd McCaslin 32:15-34:7, 35:21-36:1.
[55] BSCM06700722580.
[56] BSCM04700013329 (emphasis added).
[57] BSCM04700139872, BSCM04700139874, SECANTBSC00005688.

reaching an informed decision on whether to use the product. Hence, the MSDS, including the information about the properties of the polypropylene used in the Mesh Products, provided information relevant to the risk-benefit analysis – BSC should have provided the MSDS information to physicians to enable a full and complete risk-benefit analyses with patients.

Given the information available to BSC concerning the properties of polypropylene, coupled with the explicit warning and other contents of the MSDS, at a minimum, BSC should have conducted clinically relevant testing to determine if naturally occurring conditions in the vagina could cause polypropylene used in the BSC Mesh Products to alter the inside the woman's body (as well as other complications), and if so, what materials are released into the body as a result, and what impact would those materials have on the body.

BSC did not undertake any long-term testing to determine whether or not these warnings on the polypropylene resin manufacturers' MSDS were associated with long term consequences for permanent human use. There is sufficient evidence that polypropylene in the right circumstances can be altered and these circumstances are readily found in the female vagina and pelvis. There is also sufficient evidence that the type of polypropylene used by BSC in their BSC Mesh Products was not suitable for or made to be implanted permanently in the human body. Therefore, any polypropylene implanted in the female pelvis will expose the polypropylene to both chemical and biological alteration. It is with a reasonable degree of medical and scientific certainty the complications associated with the use of polypropylene products are the direct result of exposure to chemical and biological alteration of the BSC Mesh Products meshes and therefore the manufacturer's warning is a reasonable prohibition against the use of these products.

3. *Chronic Foreign Body Reaction*

The human body has a natural and predictable "host defense response" to any scientifically accepted foreign object placed inside of it. Whether a splinter, a bacteria or a medical device such as surgical mesh, the human body will send white blood cells to attack the invader and, if the products of inflammation cannot ward off or destroy the invader, the initial acute inflammatory phases is followed by a chronic inflammatory phase. Therefore, with the placement of a permanent surgical mesh in human tissues, there will be a chronic or permanent foreign body reaction to the implant, as well as a chronic inflammatory response by the body.[58]

[58] Klinge et al., *Shrinking of Polypropylene Mesh In Vivo: An Experimental Study in Dogs*, 164 EUR. J. SURG. 965-69 (1998); Klinge et al., *Foreign Body reaction to Meshes Used for the Repair of Abdominal Wall Hernias*, 164

For the reasons set forth above, it is my opinion to a reasonable degree of medical certainty that the polypropylene mesh in the BSC Mesh Products creates a chronic foreign body reaction which can lead to severe complications in patients, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, dyspareunia that can be chronic, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, bladder and urethra, pelvic abscess formation, risk of infection and/or the need for additional surgeries, among others. As a result, the polypropylene in the BSC Mesh Products is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women.

4. *Infections / Bio-films*

The transvaginal placement of polypropylene products, like the Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Prefyx, Pinnacle, and Uphold products, violates a fundamental tenet of surgical teachings because the procedures require placement of permanent implant through a non-sterile or "clean contaminated" field – the vagina. Because surgeons cannot sterilize the vagina, implantation through the vagina is contraindicated for every procedure and implantation.

The weave of the Mesh Products produces very small interstices which allow bacteria to enter and hide from host defenses designed to eliminate them. The bacteria can secrete an encasing polysaccharide slime (biofilm), which further shields the bacteria from destructive white blood cells and macrophages.[59] BSC knew or should have known that Biofilm increases the foreign body reaction, which results in chronic infections, chronic inflammation, erosions, and mesh and scar contracture.[60] Indeed, BSC expressed concerns about using a synthetic mesh through a transvaginal route in 1996:

> Transvaginal Approach - Although this approach sounds good conceptually, there were several clinical and mechanical concerns which were raised. . . . B. Infection

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EUR. J. SURG. 951-60 (1998); Klosterhalfen et al., *The Lightweight and Large Porous Mesh Concept for Hernia Repair*, 2 EXPERT REV. MED. DEVICES 103 (2005); Binnebosel et al., *Biocompatibility of prosthetic meshes in abdominal surgery*, 33 SEMIN. IMMUNOPATHOL. 235-43 (2011); *see also* BSCM09400034031.

[59] Osterberg et al., *Effect of Suture Materials on Bacterial Survival in Infected Wounds: An Experimental Study*, 145:7 ACTA. CHIR. SCAND. 431-34 (1979); Merritt, *Factors Influencing Bacterial Adherence to Biomaterials*, 5 J. BIOMAT. APPL. 185-203 (1991); An, *Concise Review of Mechanisms of Bacterial Adhesion to Biomaterial Surfaces*, 43 J. BIOMED. MATER. RES. 338-348 (1998); The TVM Group: J. Berrocal et al., *Conceptual advances in the surgical management of genital prolapse*, 33 J. GYNECOL. OBSTED. BIOL. REPROD. 557-87 (2004).

[60] BSCM07200000026; BSCM04800065537; BSCM04200068587; BSCM06000044463; BSCM06100068344; BSCM06300021197.

> concerns due to the direct path from vagina to bone. . . . D. Dr. Appell suggested a cautious approach to this technology until some of these questions are resolved.[61]

Despite this early concern, Boston Scientific did not address, study or research the question of infection from the transvaginal approach before marketing and selling the Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Pinnacle, and Uphold products.

Importantly, the biofilm protects the bacteria surrounding the mesh fibers against the body's host defense response (white blood cells), which destroy foreign invaders like bacteria. Thus, the weave induces the creation of a shield for bacteria entrained in the woven mesh against the body's defenses, preventing the body from fighting off the infective agents within the mesh.

The large surface areas of BSC's Mesh Products promotes wicking of fluids and bacteria. The large surface area becomes a "bacterial super highway" because the bacteria that attach themselves to the mesh during the insertion process thrive in this safe haven.[62] Additionally, the large surface areas of mesh implants provide many places for bacteria to hide from host defenses, leading to numerous complications.[63]

Numerous peer-reviewed journal articles describe secondary-mesh related infections and the dangers of implanting surgical mesh in a clean / contaminated field. Dr. Shah and his colleagues reported on the "Bacteriological Analysis of Explanted Transvaginal Meshes," which examined explanted samples of SUI slings and POP meshes. Of the 50 mesh explants examined, 52% of those explanted due to pain contained infused pathogenic organisms, 20% of those explanted due to vaginal erosions contained pathogenic organism, and 83% of those explanted due to urinary tract erosions contained pathogenic organisms.[64]

The surface area of meshes increases when polypropylene particles separate from the surface of mesh fibers due to degradation, *see* discussion *supra*. The expansive surface areas provide even larger areas for bacterial adherence to the mesh, more elution of toxic polypropylene and toxic compounds from the polypropylene, all of which increase the body's inflammatory

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[61] BNG01000262; BNG01000210.

[62] Klinge et al., *Do Multifilament Alloplastic Meshes Increase the Infection Rate? Analysis of the Polymeric Surface, the Bacteria Adherence, and the In Vivo Consequences in a Rat Model*, 63 J. BIOMED. MATER. RES. 765-71 (2002); Vollebregt et al., *Bacterial Colonisation of Collagen-Coated Polypropylene Vaginal Mesh: Are Additional Intraoperative Sterility Procedures Useful?*, 20 INT. UROGYN. J. 1345-51 (2009).

[63] *See* Klinge (2002); Vollebregt (2009).

[64] Shah et al., *Bacteriological Analysis of Explanted Transvaginal Meshes (Abstract 1144)*, 189 J. UROL. e467 (2013).

reaction and intensity of the fibrosis.[65] In addition, the cracking mesh surfaces also provide safe harbors for infectious bacteria to proliferate.

Therefore, it is my opinion to a reasonable degree of medical certainty that the Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Prefyx, Pinnacle, and Uphold products are susceptible to biofilm formation due to the weave of the mesh allowing the infiltration, harboring, and protection of bacterial contaminants; the degraded mesh surface harboring bacteria, the passage through and into a clean/contaminated field, and after exposure/erosion of the mesh into the vagina or other organs, further contamination of the mesh with a multitude of vaginal flora occurs that further increases the risk of harmful and recurrent infections in women. Accordingly, the Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Prefyx, Pinnacle, and Uphold products are not safe for their intended purpose of implantation into a woman's pelvic tissues and can lead to severe complications in patients, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, dyspareunia that can be chronic, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, bladder and urethra, pelvic abscess formation, risk of infection and/or the need for additional surgeries, among others. All of these complications can be permanent. As a result, BSC failed to act as a reasonable and prudent medical device manufacturer by manufacturing and selling its mesh in a permanent prosthetic implant.

5. *Fibrotic Bridging*

Fibrotic bridging occurs when the fibers surrounding the pores of the mesh are too close together to allow the tissue in the pore enough room to recover from the trauma of tissue damage due to implanting a surgical prosthetic device. Pores that are large enough for good, newly vascularized tissue tend to be filled with fatty tissue versus small pores that become filled with scarred or fibrotic tissue. In those instances, the scar forms across the pores or "bridges" from one side of the pore to the other. This can occur either due to the granulomas around the mesh fibers joining together or due to densely-formed fibroblast plugs between these granulomas. Either way, such bridging can lead to the creation of a rigid, scar plate that can encapsulate the mesh with scar tissue. Simply put, small mesh pores that cause fibrotic bridging turn the mesh into a solid sheet

[65] Jongebloed (1986); Sternschuss (2012); Clave (2010).

of scar tissue and there is no space or room for tissue to grow into the mesh, which is the intended purpose of the mesh. The fibrotic bridging and scar plate prevents tissue in-growth and causes complications, including, among other things, pain with the rigid mesh, shrinkage, contraction of the mesh, erosions due to mechanical irritation in the tissue of a rigid, scar-plated mesh, nerve entrapment, chronic pain and dyspareunia. [66]

In summary, for the reasons set forth above, it is my opinion to a reasonable degree of medical certainty that the polypropylene mesh in the BSC Mesh Products causes fibrotic bridging in the body, resulting in an increased inflammatory response and alteration to the architecture and function of the tissues in the female pelvic floor, leading to a multitude of injuries, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, dyspareunia that can be chronic, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, bladder and urethra, pelvic abscess formation, risk of infection and/or the need for additional surgeries, among others. As a result, the polypropylene in BSC's Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Prefyx, Pinnacle, and Uphold mesh is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women.

6. *Mesh Contracture / Shrinkage*

Mesh contracture or shrinkage takes place after the implantation of mesh in the delicate and sensitive tissues of the human vagina and pelvis. Contracture or shrinkage relates to the wound healing process from the surgical trauma of implanting a foreign body made of polypropylene in the vagina and pelvis. By 1998, scientific studies demonstrated that polypropylene mesh contracts or shrinks up to 30-50%.[67] The literature reports an association between shrinkage or contracture and scar plate formation.[68] In *Marcus-Braun et al.*, the researchers reported that mesh shrinkage is one of the most frequent mesh-related complications described in the literature. The intense foreign

[66] Klosterhalfen (2005).

[67] Klinge et al., *Shrinking of Polypropelene Mesh in Vivo: An Experimental Study in Dogs*, 164 EUR. J. SURG. 965-69 (1998); Jacquetin et al., *Complications of Vaginal Mesh: Our Experience*, 20 INT. UROGYN. J. 893-96 (2009); Tunn et al., *Sonomorphological Evaluation of Polypropylene Mesh Implants After Vaginal Mesh Repair in Women with Cystocele or Rectocele*, 29 ULTRASOUND OBSTET. GYNECOL. 449-52 (2007).

[68] *See* Feiner et al., *Vaginal mesh contraction: definition, clinical presentation, and management*, 115(2:1) OBSTET. GYNECOL. 325-30 (2010); Maher et al., *Surgical management of pelvic organ prolapse in women*, 4 COCHRANE DATABASE SYST. REV. CD004014 (2013); Rogo-Gupta et al., *Trends in surgical mesh use for pelvic organ prolapse from 2000 to 2010*, 120(5) OBSTET. GYNECOL. 1105-15 (2012).

body reaction to the polypropylene causes a scar plate to form around and encapsulate the implants, which in turn shrinks and contracts the polypropylene.[69] The amount of mesh shrinkage or contracture is directly correlated to the extent of a patient's foreign body reaction to the mesh.[70] Degradation of polypropylene meshes also results in shrinkage and contraction of the material because the degraded devices weaken or embrittle as they degrade.[71] Contraction or shrinkage is also closely related to the pore size of a mesh. Mesh with small pores results in fibrotic bridging leading to scar plates, mesh encapsulation, and shrinkage or contraction of the mesh, which compounds and combines with the effect of the normal wound healing process that is already occurring in the tissue.[72] Research shows that contraction or shrinkage draws nerves close to the mid-urethral sling mesh whether implanted using the transobturator[73] or retropubic approach.[74] *Sternschuss et al.* (2012) reported that the degradation process causes "mesh shrinkage and chronic pelvic pain."[75]

It is my opinion to a reasonable degree of medical certainty, based on work with internal and external experts and consultants in the late 1990s, multiple internal documents and articles, and the scientific literature as a whole, BSC was or should have been aware that shrinkage of its mesh not only could, but would, occur and that this shrinkage could lead to painful complications in women implanted with Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Prefyx, Pinnacle, and Uphold. The complications associated with shrinkage or contracture that were known or knowable to BSC include multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, dyspareunia that can be chronic, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, bladder and urethra, pelvic abscess formation, risk of

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[69] *See* Marcus-Braun et al., *Mesh Removal Following Transvaginal Mesh Placement: A Case Series of 104 Operations*, 21 INT. UROGYNECOL. J. 423 (2010).

[70] *See* Klosterhalfen (2005); Cobb et al., *The Argument for Lightweight Polypropylene Mesh in Hernia Repair*, 12 SURGICAL INNOVATION 63 (2005).

[71] Clave (2010); Costello et al., *Materials Characterization of Explanted Polypropylene Hernia Meshes*, 83B J. BIOMEDICAL MATERIALS RES. PART B 44 (2007); *see also* Costello et al., *Characterization of Heavyweight and Lightweight Polypropylene Prosthetic Mesh Explants from a Single Patient*, 14 SURGICAL INNOVATION 168 (2007).

[72] *See* BSCM04700136392; BSCM07400017395; BSCM06100068344.

[73] Corona et al., *Tension-free Vaginal Tapes and Pelvic Nerve Neuropathy*, 15:3 J. MIN. INVAS. GYNECOL. 262-67 (2008); Parnell et al., *Genitofemoral and Perineal Neuralgia after Transobturator Mid-urethral Sling*, 119 OBSTET. GYNECOL. 428-31 (2012).

[74] Heise et al., *Mesh Inguinodynia: A New Clinical Syndrome After Inguinal Herniorrhaphy?*, 187:5 J. AM. COLL. SURG. 514-18 (1998); Voeller et al., *New Developments in Hernia Repair*, 11 SURG. TECHNOL. INTL. 111-16 (2003).

[75] Sternschuss (2012), 188 J. UROL. at 31.

infection and/or the need for additional surgeries, among others. As a result, the polypropylene in BSC's Mesh Products is not suitable for its intended application as a permanent prosthetic implant to treat SUI or POP in women.

7. *BSC Internal Documents Concerning Mesh's Defective Properties Are Consistent With and Support My Opinions Expressed Herein*

BSC's internal documents are consistent with the opinions I have offered in this case and provide support therefore. The following discussion of my review of internal corporate documents is provided for the purpose of explaining the basis for my opinions expressed herein.

For example, in September 2008, BSC asked Dr. Joseph Macaluso to conduct a literature search and analysis report in order to determine the following: frequency and causes of mesh complications; severity of mesh complications; treatment of complications; proactive measures to avoid complications; what long term risks exist; and what product enhancements might reduce future complications.[76] Dr. Macaluso provided them with a report that included among other things: all mesh use increases complications; eroded, infected mesh must be removed; use mesh only as needed and if really necessary; less use of transvaginal mesh is better; lesser amount/volume placed when implanted is better; and larger pore size is better and preferred.[77] He further stated that he also identified that pore size has everything to do with polypropylene safety. He identified that along with increased numbers of transvaginal mesh repairs being performed there was a corresponding increase in referrals for complications related to the mesh use. One of the most common complications is extrusion of the mesh into the vagina and these observations support the theory of polypropylene mesh shrinkage as a consequence of the incorporation of the biomaterial to the scarring tissue.[78]

Similarly, in a power point presentation, Dr. Dennis Miller, who receives royalties and consulting fees from BSC, states that "The best graft is no graft" and that there is a need to minimize stiffening/contraction/folding of polypropylene mesh, along with reducing contamination and degradation. In the same presentation BSC was told that with degradation, toxic compounds are released and that roughness in mesh causes wicking. Dr. Miller also states in that PowerPoint that elasticity "is no guarantee, it is gone during healing". In this same presentation, BSC was told that there is bacterial adherence to mesh, that adherence is directly related to

[76] BSCM06500079785.
[77] BSCM04400163499.
[78] *Id.*

available surface area, and that better surgeon training was necessary for the mesh products. These facts are consistent with the information that was available in the literature.[79]

Furthermore, in October 2010, BSC employees, including Janice Connor, Director of Clinical Programs, attended the AUGS Inaugural Research Summit that included presentations from various clinicians, including Dr. Mickey Karram, whom BSC considered to be "a world-renowned urogynecologist" and was a Key Opinion Leader for BSC.[80] Connor's notes from Dr. Karram's presentation include the "arguments against mesh" which listed "Not a lot of data, Costly, Concerns about future complications, Potential worsening of functional derangements, Legal implications."[81] Connor's notes from Dr. Karram's presentation also state that the "ideal graft" is "Biocompatible, Resistant to mechanical stress or shrinkage, Available and inexpensive, Easily retains suture, Not associated with donor site morbidity, Not inflammatory, infectious or carcinogenic".[82] Connor's notes also detail industry influence on pelvic repairs, "Industry plays a big role; has proposed and promoted perceptions that may be inaccurate; say that conventional repairs ultimately fail, that anatomic durability is ultimate goal, that prolapse repair is analogous to SUI (can do cookie cutter), science supports mesh . . . Physician influenced by industry, financial reward for certain products ($500 more on vag repair if you use mesh)."[83] Connor's notes from Dr. Karram's presentation also note that there are "Significant training gaps - many novice surgeons that have dabbled little in this area who are performing these procedures; current training mechanisms are ridiculous, the idea that you go to a cadaver lab and learn how to pass a trocar, how to place something and feel that you can go back and do this is amazing . . . Safety continues to be a problem, what are acceptable risks and complications, can still have severe life threatening or debilitating outcomes."[84] Connor's notes further stated that "everybody has different weight and pore size – we don't know if these differences are clinically relevant."[85] Connor's notes from Dr, Karram's presentation also state that, "National standards needed - training programs, dissemination needed of factual information regarding guidelines physicians should try, discourage low volume surgeons from doing advanced surgery, disseminate the fact that docs

[79] BSCM06100068344.
[80] Dep. of Janice Connor Dep. (Vol. 1) 94:20-99:9.
[81] BSCM04800072360.
[82] *Id*.
[83] *Id*.
[84] *Id*.
[85] *Id*.

should have an understanding of pelvic anatomy as well as skills prior to performing pelvic floor surgery, there's a lack of understanding in anatomy."[86]

By 2012, BSC had developed a Lite mesh and drafted a Training Plan and Facilitator Guide to present at National Sales Meetings.[87] In that document, BSC cited literature that is consistent with, and supports, the opinions that I have offered herein. For example, BSC cited literature to support the following propositions:

- "Given that polypropylene mesh is not inert within the human body, that mesh shrinkage of up to 20% to 50% occurs, that large pore size is important for fibrous tissue ingrowth and mesh incorporation into host tissues, that surface area is directly related to subsequent infection and complications, newer meshes should be designed with these factors in mind."

- "It has been observed that low surface area meshes significantly reduce foreign body reactions. A reduced foregin [sic] body reaction correlates with decreased rates of shrinkage, connective tissue formation (scarring) and bridging. . . . lightweight meshes with large pores appear to have less serious complications overall."

B. BSC's Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Prefyx, Pinnacle, and Uphold Products Lack Adequate Studies To Establish Safety And Effectiveness For Permanent Human Implantation To Treat SUI or POP.

A reasonable and prudent medical device manufacturer should have adequate safety data to support its products before urging surgeons to use them permanently on patients.[88] In 1999, BSC acknowledged the duty to establish safety on transvaginal mesh products prior to market. Indeed, BSC temporarily withdrew from the synthetic mesh market in 1999 when it voluntarily withdrew the Protegen sling from the U.S. market. BSC withdrew the Protegen, in part, after suspending a BSC sponsored clinical trial that observed an erosion rate of approximately 30%. From the Protegen lesson, BSC pledged to collect clinical data on synthetic transvaginal mesh products in the future before marketing them to the public. In fact, BSC acknowledged that synthetic

[86] BSCM04800072360.

[87] BSCM06100209440.

[88] Boyles et al., *Complications associated with transobturator sling procedures*, 18 INT. UROGYNECOL. J. 19-22 (2007); Hogewoning et al., *The introduction of mid-urethral slings: an evaluation of literature*, 26(2) INT. UROGYNECOL. J. 229-34 (2015) ("clinicians and their professional organizations should only choose devices that have adequate clinical data to support their efficacy and safety"); Abrams et al., *Synthetic Vaginal Tapes for Stress Incontinence: Proposals for Improved Regulation of New Devices in Europe*, 60 EUR. UROL. 1207-1211 (2011) ("Manufacturers' responsibilities should include the following tasks: testing the device thoroughly, including carrying out appropriate clinical trials, before placing on market.") ("The need for randomized controlled trials (RCTs) at an early stage of development of any new device, with significant new features compared with existing tapes, was felt be essential. The clinicians expressed regret about the number of low-quality studies, usually case series, published in the literature.").

transvaginal mesh products cannot be safely launched without clinical data establishing safety. Nevertheless, BSC did not conduct any clinical trials on the Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Pinnacle, and Uphold products prior to marketing the products as a permanent medical implant in women.[89] In contradiction to the lessons BSC learned with the Protegen, BSC claims biocompatibility testing and the scientific literature establish the safety and efficacy of a permanent mesh implant.[90]

However, BSC employees raised concerns about the lack of clinical data on the Mesh Products.[91] Janice Connor testified that the public and physicians need data on the products to enable a true risk/benefit analysis.[92] In a 2009 email to John Pedersen, BSC's division president, Connor described the clinical data as "dramatically lacking in published data on a majority of . . . women's health products, yet a large amount of funding would be required to manage and design these trials."[93] Despite the need, BSC had not sponsored a mesh versus non-mesh study as of 2013.[94] Nor has BSC acted on Connor's 2009 recommendation to conduct a biologic versus synthetic mesh study.[95]

BSC's employees readily admit the duty to establish safety with clinical trials when launching a synthetic transvaginal mesh product. As the inventor of the Pinnacle device testified, the Pinnacle required clinical studies to determine the device's clinical effectiveness in treating POP.[96] Janice Connor, BSC's Director of Clinical Affairs, testified that "it is the company's responsibility to create directions for use, along with the FDA" and the indications for use must be accurate.[97] She acknowledged BSC's "responsibility [to] ensure that our products being marketed are safe."[98] Further, Connor testified "the need for supportive data for new products is essential, especially in light of issues seen with similar devices" and the need "to have the budget behind it in order to be well executed."[99]

[89] Dep. of Donna Gardner 19:9-13; Dep. of John Sherry 100:10-16.
[90] Dep. of Doreen Rao 44:20-45:6, 45:14-46:5.
[91] BSCM04700020525; BSCM00400001798; BSCM04800066324; BSCM06100053666.
[92] Connor Dep. (Vol. 1) 101:1-9.
[93] Connor Dep. (Vol. 1) 174:6-176:6, 180:1-8 (discussing Exhibit 490)
[94] Connor Dep. (Vol. 1) 182:10-18 (discussing Exhibit 490).
[95] Connor Dep. (Vol. 1) 182:19-183:1 (discussing Exhibit 490).
[96] Dep. of Dennis Miller 126:12-127:21.
[97] Connor Dep. (Vol. 1) 112:19-22.
[98] Connor Dep. (Vol. 1) 113:9-14.
[99] Connor Dep. (Vol. 1) 142:4-13.

It is my opinion to a reasonable degree of medical and scientific certainty that a dead person or a simulated model cannot produce relevant, reliable and dispositive information regarding performance of a device in an alive human being. Instead, obtaining this information requires human studies. However, when considering clinical trials, BSC identified on the risks, "[m]oney; Potential for negative outcome; uncontrollable data; underreporting of safety events," rather than patient safety.[100] The facts here show BSC neglected to analyze the material science of the Mesh Products' effects during implantation on a living human being or in a cadaver.[101] Furthermore, BSC lacked any data on long term the long terms safety or effectiveness profile of the Mesh Products as of September 2008.[102] As of 2015, BSC had never sponsored a completed clinical trial (other than a registry with flawed data) for the Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Prefyx, Pinnacle and Uphold products.[103]

The scientific literature contains significantly insufficient publications on the safety or effectiveness of the Mesh Products. A BSC commissioned literature review in 2008 illustrates the opposite – the literature established the Mesh Products as unsafe surgical options:

- **All mesh use increases complications: such as discharge, dyspareunia, erosion, infection**
- **Eroded, infected mesh must be removed**
- **Use mesh only as needed *AND IF REALLY* necessary**
- **Less use is better**
- **Lesser amount/volume placed when used is better**
- **Larger pore size is better and preferred**[104]

The literature lacked sufficient safety and effectiveness evidence for BSC to market the SUI and POP products. The Scottish Independent Review determined the evidence on the safety and effectiveness of polypropylene mesh for SUI and POP still insufficient in March 2017.[105]

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[100] BSCM04800073303.

[101] Dep. of James Goddard (Vol. 3) 98:2-7, 98:18-23.

[102] BSCM06500079785.

[103] Connor Dep. (Vol. 1) 101:15-104:7; Dep. of Janice Connor (Vol. 3) 65:21-71:21, 73:7-74:3, 77:17-78:7, 244:21-25.

[104] BSCM04400163499 (emphasis in original).

[105] *See* SCOTTISH INDEPENDENT REVIEW, THE USE, SAFETY AND EFFICACY OF TRANSVAGINAL MESH IMPLANTS IN THE TREATMENT OF STRESS URINARY INCONTINENCE AND PELVIC ORGAN PROLAPSE IN WOMEN (2017); *but see Update on Vaginal Mesh for Prolapse and Incontinence*, AMERICAN UROGYNECOLOGIC SOCIETY, (Feb. 13, 2018, 10:07 AM), https://www.augs.org/update-on-vaginal-mesh-for-prolapse-and-incontinence/; Souders et al., *The Truth Behind Transvaginal Mesh Litigation: Devices, Timelienes, and Provider Characteristics*, 24(1) FEMALE PELVIC MED. RECONSTR. SURG. 21-25 (2018).

1. *Advantage, Advantage Fit, Lynx, Obtryx, Prefyx, & Solyx*

In 2011 – nine years after first marketing the Advantage device – the scientific and medical literature lacked any long-term data on the Advantage mesh used in Advantage, Advantage Fit, Lynx, Obtryx, Prefyx, and Solyx products.[106] In 2015, Ms. Connor claimed that over thirty (30) studies on the Advantage mesh existed in the scientific literature.[107] Ms. Connor also alleged thirteen (13) studies cover the Advantage and Lynx products,[108] while twenty-two (22) examine the Obtryx product.[109] However, only three (3) BSC sponsored clinical studies, one (1) of which is unpublished, exist on the Advantage, Advantage Fit, Lynx, Obtryx, Prefyx, and Solyx products.[110] BSC sponsored two (2) clinical studies on the Prefyx, and one (1) clinical study on the Advantage and Obtryx. As of 2015, no BSC sponsored clinical studies exist on the Lynx or Solyx devices.[111] Although randomized controlled trials ("RCTs") represent the gold standard of clinical testing, [112] BSC did not test the Advantage, Advantage Fit, Lynx, Obtryx, Prefyx, and Solyx products in RCTs – nor does any data from RCTs on the products otherwise exists in the medical or scientific literature.[113] In addition, the medical and scientific literature contains no publications on long-terms RCTs with safety as the primary endpoint for any of BSC's polypropylene devices.[114]

By contrast, other manufacturers of mid-urethral slings rely on hundreds of published studies, articles, and trials to establish the effectiveness of the products. In my experience, it is exceedingly unusual to have such a limited body of medical and scientific literature to support the safety and effectiveness of a permanently implantable medical device. This very limited literature raises serious concerns about the safety and effectiveness of the Advantage, Advantage Fit, Lynx, Obtryx, Solyx and Prefyx products. The literature on these products is limited not only in quantity, but also in quality. Indeed, the literature lacked any data collected through the gold standard of

[106] Dep. of Janice Connor (Vol. 4) 409:23-411:18.
[107] *Id.* 501:22-502:12.
[108] *Id.* 511:9-512:10 (discussing Exhibit 1333 describing studies for the Advantage and Lynx products).
[109] *Id.* 521:8-13 (discussing Exhibit 1335 describing studies for the Obtryx product).
[110] Connor Dep. (Vol. 3) 73:7-12.
[111] *Id.* 65:21-67:4.
[112] *Id.* 65:1-19.
[113] *Id.* 73:7-74:13.
[114] *Id.* 204:6-10.

clinical testing – RCTs – on BSC's Mesh Products for SUI.[115] Since 2007, there have been few RCTs on the remainder of BSC's Mesh Products.

In a 2006 publication comparing the Advantage mesh to the mesh used in Ethicon's TVT, researchers conducted a histological examination of both meshes to determine if tissue reacted the same to both meshes.[116] Ms. Connor testified, the article's conclusion shows the TVT's mesh is not equivalent to the Advantage mesh.[117] The study reported significant differences between tissue responses to the TVT's mesh and the Advantage mesh. Specifically, the researchers discovered the Advantage mesh induces more inflammation and fibrosis in tissue than the mesh in the TVT. Because of these differences, the authors conclude that new slings introduced after the TVT require prospective and epidemiologic studies to support use.[118] In 2008, another publication cautioned about unforeseen complications that result from modifications to existing sling technologies:

> as we have seen with the advancements that have evolved over the last decade, there can sometimes be confounding side effects and unforeseen consequences caused by the changes created by new and improved technologies. . . . . It is too early to comment on the mini-slings as to any possible unforeseen complications that may occur when the product is implanted in a volume of patients and thus further study via RCT's [randomized controlled trials] are indicated.[119]

Applying the findings to the then new mini-sling technology, including BSC's Solyx, the authors concluded the modification necessitated further study in an RCT to unveil unforeseen complications.[120] In short, the literature urges manufacturers that modify existing polypropylene transvaginal mesh products to study the product in a clinical setting to confirm safety and effectiveness.

In their 2010 article investigating the TVT and Advantage slings, *Do the Advantage slings work as well as the tension-free vaginal tapes?*, the authors found "[t]here is currently no data on the safety and efficacy of the Advantage sling despite its widespread use."[121] The authors also stated, "[a]ccording to Boston Scientific (personal communication), since its introduction in 2003,

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[115] *Id.* 73:7-74:13, 204:6-10.

[116] Bazi et al., *Polypropylene Mid-urethral Tapes Do Not Have Similar Biologic and Biomechanical Performance in the Rat*, 51 EUR. UROL. 1364-1375 (2007).

[117] Connor Dep. (Vol. 4) 621:14-18.

[118] Bazi et al., 51 EUR. UROL. 1364-1375.

[119] Moore et al., *Minimally invasive treatment for female stress urinary incontinence*, 3(2) EXPERT REV. OBSTET. GYNECOL. 257-72 (2008).

[120] *Id.*

[121] Lim et al., *Do the Advantage slings work as well as the tension-free vaginal tapes?*, 21(9) INT. UROGYNECOL. J. 1157-1162 (2010).

over 82,000 Advantage slings have been implanted worldwide. However, Medline search failed to find any outcome data with this new form of retropubic MUS."[122] The publication reports a two times higher rate of failure when an inexperienced surgeon placed either sling, along with higher rates of overactive bladder and voiding dysfunction in the Advantage group. The authors postulated this trend was related to the stiffer and less elastic midportion or detanged portion of the Advantage mesh (as compared to the TVT).[123] As of 2015, BSC had never conducted a clinical study or trial to learn about the safety or effectiveness of the Advantage mesh's detanged mid-urethral portion used in each of the SUI Mesh Products.[124]

If anything, the available literature demonstrates that the Advantage, Advantage Fit, Lynx, Obtryx, Solyx and Prefyx products are inferior to other manufacturers' mid-urethral slings. BSC's only pre-market clinical study on any of the Mesh Products demonstrated the Prefyx as an unsafe option to treat SUI.[125] Dr. Paul Tulikangas, a co-author of the AUGS statement on mid-urethral slings, raised concerns with BSC in 2011 about the lack of clinical data supporting the Mesh Products, and the inferior results reported in the limited literature available on BSC's sling products. In that e-mail exchange, BSC acknowledged, "[t]o be honest, there has not been a large desire to complete research in these areas previously so the support we have, although effective, is minimal."[126] In response, Dr. Tulikangas disagreed with BSC: "[u]nfortunately the limited data here shows your product to be inferior with more groin pain (15%) and a high erosion rate (4%)."[127] Dr. Tulikangas criticized three medical publications on BSC slings in reaching his conclusion:

1. Ross et al., *Transobturator tape compared with tension-free vaginal tape for stress incontinence: a randomized controlled trial*, 114(6) OBSTET. GYNECOL. 1287-94 (2009) – "This is a well done study. The conclusions state that the Boston Scientific Sling should not be used secondary to the high rates of pain compared to the TVT."[128]
2. Lim et al., *Do the Advantage slings work as well as the tension-free vaginal tapes?*, 21(9) INT. UROGYNECOL. 1157-62 (2010) – "Poor quality study but it concludes

[122] *Id.*
[123] Renganathan et al., *A series of Advantage suburethral slings*, 31(6) J. OBSTET. GYNECOL. 521-523 (2011).
[124] Connor Dep. (Vol. 3) 166:13-23.
[125] *See* discussion *supra* Part III.B.4. on Prefyx pre-market clinical study and results.
[126] BSCM06100066377.
[127] BSCM06100066376.
[128] *Id.*

'more over active bladder and voiding issues' with the Advantage sling, 'may be related to the slightly stiffer nature' of the Advantage."[129]

3. Noblett et al., *Lynx mid-urethral sling system: a 1-year prospective study on efficacy and safety*, 19(9) INT. UROGYNECOL. J. PELVIC. FLOOR. DYSFUNCT. 1217-21 (2008) – "4% erosion rate is higher than most MUS trials-very concerning."[130]

The medical literature BSC cites to support the Mesh Products also contains significant reliability issues. For example, BSC funded or supported many of the "studies." This funding was not always disclosed. The Rengantahan study fails to disclose that BSC funded the study.[131] Another author in the Vu study was a consultant for BSC who received royalties from BSC.[132]

BSC also sponsored studies even after determining it was not a permissible sponsor: "since this is an ISR, we/BSC are not allowed to perform any 'sponsoring' functions on this project, therefore Compass Point is a Contract organization working with Dr. Miller on the execution of this trial. Sara Kivolowitz and Lori Nesbitt are our contacts at Compass Point. That said, they need your help."[133] Although "not allowed to perform any sponsoring functions on the project," emails show BSC paid for and required particular parameters for the Rosenblatt study in 2012:

> Hell no. I don't agree w/their rationale at all. Our contract adds up to $55,350 (the one you sent 12/9), theirs adds up to $83,025 ($27,675 over). I see her note below about the amount of work needed to do an abstract, etc. but that is not worth $27,675. I refuse to pay them anymore for these milestones we clarified in the new contract. We had always talked about an abstract and a publication. What did they think they would give us a draft publication and that would be it???[134]

BSC also approved and edited the final publication.[135] The final publication did not acknowledge BSC's funding or editorial commentary.[136] As an additional flaw, BSC also relies on studies that include unreliable data. These studies include non-peer reviewed abstracts of meeting

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[129] *Id.*
[130] *Id.*
[131] Renganathan (2011).
[132] Vu et al., *Minimal mesh repair for apical and anterior prolapse: initial anatomical and subjective outcomes*, 23(12) INT. UROGYNECOL. J. 1753-61 (2012).
[133] BSCM0480005544.
[134] BSCM04800163642.
[135] *Id.*
[136] Rosenblatt et al., *Multi-Center Retrospective Clinical Evaluation Of The Long Term Outcomes Following Pelvic Organ Prolapse Repair Using Pinnacle PFR Kit (Anterior Apical)*, AM. UROGYN. SOC. ANNUAL MEETING: CHICAGO, IL., Poster (Oct. 3-6, 2012).

presentations with short follow up periods,[137] and flawed data.[138] Despite being aware that the data was flawed, BSC failed to issue a retraction.[139] The authors of the flawed abstract even acknowledge that "these results may not be predictive of data from other sling registries."[140]

2. *Pinnacle & Uphold*

When BSC withdrew the Pinnacle and Uphold from the market in the United States, no prospective, randomized, controlled clinical trials on the products existed in the scientific or medical literature. In 2015, Ms. Connor claimed that twenty-seven (27) studies on the Pinnacle or Uphold existed in the scientific literature.[141] However, "[z]ero" BSC sponsored clinical trials on the Pinnacle or Uphold existed in the scientific literature in 2015.[142] Further, only two (2) full-length, peer-reviewed articles on the Pinnacle existed in the scientific literature as of 2015.[143] For the Uphold, only four (4) full-length, peer-reviewed articles on the Uphold existed in the medical literature as of 2015.[144] In 2017, the National Institute for Health and Care Excellence ("NICE") concluded the available evidence actually demonstrates serious safety concerns: "[c]urrent evidence on the safety of transvaginal mesh repair of anterior or posterior vaginal wall prolapse shows there are serious but well-recognised safety concerns."[145]

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[137] Litwiller et al., *Long Term Efficacy And Safety of the Obtryx (Boston Scientific Corp.) Sling for Treatment of Stress Urinary Incontinence In A Community Setting: An Analysis Of Outcomes and Quality of Life*, J. PELVIC. MED. & SURG., Poster 109 (Sept. 2009); Serels et al., *Preliminary findings with the Solyx single-incision sling system in female stress urinary incontinence*, 21(5) INT. UROGYNECOL. J. 557-61 (2010); Lind et al., *PrePubic Mid-Urethral Sling for Stress Urinary Incontinence: Prospective Single-Arm Clinical Study of Efficacy, Safety and Sexual Function – Interim Data*, SOC. GYNECOL. SURGEONS ANNUAL MEETING: ORLANDO, FL., Poster (2007).

[138] Costa, *Comparisons of Safety and Efficacy of the Obtryx® Sling and AdvantageTM Mid-Urethral Sling for the Treatment of Stress Urinary Incontinence: Propensity Matching Results in a Large International Registry*, 17(6) J. MIN. INV. GYNECOL. S182 (2010).

[139] Dep. of Janice Connor (Vol. 2) 398:19-24, 400:21-401:7; BSCM05200000734-36.

[140] Costa (2010).

[141] Connor Dep. (Vol. 4) 554:22-555:10, 565:2-8 (discussing Exhibit 1341 listing Pinnacle studies, and Exhibit 1344 listing Uphold studies).

[142] Connor Dep. (Vol. 3) 77:22-78:7.

[143] *Id.* 245:1-7, 255:11-20 (identifying these two (2) articles: Jeffery et al., *High Risk of Complications with a Single Incision Pelvic Floor Repair Kit, Results of a Retropubic Case Series*, 25 INT. UROGYNECOL. J. 109-16 (2013); Larouche et al., *Outcomes of Trocar-Guided Gynemesh PS Versus Single-Incision TrocarLess Polyform Transvaginal Mesh Procedure*, 26(1) INT. UROGYNECOL. J. 71-77 (2015)).

[144] *Id.* 255:2-256:12 (identifying these four (4) articles: Larouche (2015); Jirschele et al., *Multicenter Prospective Trial to Evaluate Mesh Augmented Sacrospinous Hysteropexy for Uterovaginal Prolapse*, 26(5) INT. UROGYNECOL. J. 743-48 (2015); Rivaux et al., *Uterovaginal Suspension Using a Bilateral Vaginal Anterior Sacrospinous Fixation with Mesh, Preliminary Results*, 22 PROG. UROL. 1077-83 (2012); Vu et al., *Minimal Mesh Repair for Apical and Anterior Prolapse, Initial Anatomical and Subjective Outcomes*, 23(12) INT. UROGYNECOL. J. 1753-61 (2012)).

[145] NAT'L INST. FOR HEALTH AND CARE, TRANSVAGINAL MESH REPAIR OF ANTERIOR OR POSTERIOR VAGINAL WALL PROLAPSE, p. 1 (2017).

In 2006, the French National Authority for Health ("HAS") evaluated the safety and effectiveness of transvaginal mesh for treatment of POP.[146] In 2006, the available literature contained insufficient data to determine the anatomical and functional viability of transvaginal mesh for treatment of POP. Hence, HAS concluded the use of transvaginal mesh for treatment of POP remained a matter of clinical research.[147] In 2017, Nice also concluded POP repair with polypropylene mesh "should only be used in the context of research."[148] Despite HAS's 2006 conclusion requiring additional clinical research on the use of transvaginal mesh to treat POP, BSC launched the Pinnacle in 2007 and Uphold in 2008 without any clinical support.

In 2009, Ms. Connor acknowledged, BSC was "dramatically lacking in published data on a majority of [its] women's health products, yet a large amount of funding would be required to manage and design these trials."[149] After two years of marketing the Pinnacle in the United States, "[t]here [were] no published journal articles on the Pinnacle."[150] Roger Goldberg, M.D., who brought the Uphold's concept to BSC, testified that safety determinations with a scientific basis required clinical evidence: "the elements of th[e Uphold] were based on theories . . . [i]f you're asking can I claim that Uphold is safer than Pinnacle, there's no head-to-head trials and I don't really have a scientific basis to say that that's factually true."[151] In 2011, the American College of Obstetricians commented on the available data for Pinnacle and Uphold indicated posterior and apical repairs: "[t]here are insufficient data on the use of mesh for the posterior or apical compartments."[152] In 2011, the FDA concluded the evidence in the medical and scientific literature was insufficient to establish the safety and effectiveness of the Pinnacle and Uphold devices to treat POP.[153]

The available literature on the Pinnacle and Uphold products actually establishes the products as unsafe options for POP treatment. In one of the full-length, peer-reviewed publications,

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[146] FRENCH NAT'L AUTH. FOR HEALTH, EVALUATION OF MESH IMPLANTS INSTALLED THROUGH THE VAGINAL APPROACH IN THE TREATMENT OF GENITAL PROLAPSE (trans., French to English) (2006) (HAS conducted this study at the request of the National College of French Gynecologists and Obstetricians and the French Association of Urology.).

[147] *Id.*

[148] NAT'L INST. FOR HEALTH AND CARE at p. 1.

[149] Connor Dep. (Vol. 1) 174:6-176:6, 180:1-8 (discussing Exhibit 490)

[150] BSCM05100112164.

[151] Goldberg Dep. 387:8-21.

[152] Committee on Gynecologic Practice Opinion, *Vaginal Placement of Synthetic Mesh for Pelvic Organ Prolapse*, 2011 AM. COLL. OBSTET. OP. NO. 513.

[153] Connor Dep. (Vol. 4) 649:3-9, 651:8-19.

the *Jeffery* article reports complications in 70% of women implanted with a Pinnacle device.[154] At the conclusion of the first peer-reviewed publication about the Pinnacle, *Jeffery* recommends the use of another device because of the Pinnacle's safety risks:

> this paper is the first clinical report on the Pinnacle device and this series highlights a number of significant concerns regarding the use of this mesh kit. Alternative devices are now available and we believe that clinicians wishing to use an apical single incision kit should consider options other than the Pinnacle kit.[155]

Of the four (4) full-length, peer-reviewed publications for the Uphold, none examined safety as the primary endpoint or provided any long-term data.[156] In a 2006 literature review of graft materials used in pelvic floor surgery, researchers investigated the use of synthetic materials, like polypropylene mesh in the Uphold, for apical suspension procedures.[157] The literature reported high rates of complications with the use of polypropylene meshes in apical suspension procedures. Specifically, the literature for these procedures revealed high rates of dyspareunia (between 25%-60%), recurrence (between 4.0%-13.3%), sacral pain (13.7%), and erosion (between 2.0%-6.7%).[158] Based on the complication rates observed in 2006 – almost two years before the Uphold's launch – the study discouraged the use of synthetic material, specifically polypropylene mesh, in apical suspension procedures.[159] In conclusion, the researchers opposed the use of graft material in pelvic surgeries until "well-powered randomized controlled trials" support the use.[160]

As of 2015, BSC has not completed any clinical trials on the Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Pinnacle, and Uphold products.[161] In my opinion, to a reasonable degree of medical and scientific certainty, issues such as chronic pain, dyspareunia, shrinkage, degradation, deformation of the mesh (folding, bending, bunching, and cording), inflammatory reactions, and impact on sexual function, bladder, and bowel function should have been studied by BSC prior to marketing. Outcomes and complications should have been resolved prior to marketing. Contingency plans should have been in place on how to manage these complications. BSC should

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[154] Connor Dep. (Vol. 3) 256:18-257:4.
[155] Jeffery et al., 25 INT. UROGYNECOL. J. at 116.
[156] *Id.* 256:18-257:4.
[157] Huebner et al., *The Use of Graft Materials in Vaginal Pelvic Floor Surgery*, 92 INT. J. GYNECOL. & OBSTET. 279-288 (2006).
[158] *Id.* at 285.
[159] *Id.* at 285-86.
[160] *Id.* at 286.
[161] Connor Dep. (Vol. 1) 101:15-104:7; Connor Dep. (Vol. 3) 65:21-71:21, 73:7-74:3, 77:17-78:7, 244:21-25.

have adequately studied the safety and effectiveness of the Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Prefyx, Pinnacle, and Uphold devices to provide scientifically based information to physicians to use in risk-benefit analyses with patients and treating patients with complications from the Mesh Products.

C. BSC Disregarded Prior Experience With The Protegen Device When Manufacturing the Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Prefyx, Pinnacle, and Uphold Products.

BSC's current issues with the Mesh Products are consistent with BSC's Protegen experience in the late 1990s. In the late 1990s, BSC marketed a mid-urethral sling with coated polyester mesh and multifilament fibers called the Protegen.[162] Indicated for the exact same use as the Advantage, Advantage Fit, Lynx, Obtryx, Solyx, and Prefyx, the Protegen was BSC's first attempt to incorporate Trelex hernia technology (made with Marlex Polypropylene) into a transvaginal device to treat SUI.[163] Like the Advantage, Advantage Fit, Lynx, Obtryx, Solyx, and Prefyx products, surgeons blindly implanted the Protegen through the vagina and into the pelvic cavity to support the midurethra. Also like the Advantage, Advantage Fit, and Lynx products, BSC's only premarket testing on the Protegen tested the device's biomechanical properties under ISO 10993 bench testing protocols.[164] Like the Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Pinnacle, and Uphold products, BSC sold the Protegen without any pre-market clinical testing that verified safety or effectiveness for permanent implantation to treat SUI.

Concerns about the Protegen sling arose internally and externally from its earliest days. In 1997, Dr. Willie Davilla raised concerns about the sling with BSC, asking "[w]hy is the Protegen sling being advertised as God's gift to anti---incontinence surgery when we haven't even really begun the study???? Doesn't seem right to run ads before data is even in, much less a number of procedures under anyone's belt. . . . I guess business runs science, shouldn't be that way."[165] While on the market, BSC received numerous complaints about the Protegen, some specifically about the seriousness of complications.[166]

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[162] Rao Dep., 79:23-81:12.
[163] JOM000297.
[164] JOM03000196.
[165] DHS05001366.
[166] DHS04001634; DHS04001643; DHS04001644; DHS01001926; DHS07001879.

BSC voluntarily discontinued the sale of the Protegen device in 1999 because of several medical complications that arose with its use.[167] First, BSC discontinued the product because "infection issues related to synthetics were rooted in the growth of bacteria within the interstices present in synthetic materials."[168] As discussed *supra* Part IV.A, BSC's Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Prefyx, Pinnacle, and Uphold also present the same infection issues for patients because of bacteria embedded within pores following transvaginal implantation. Second, BSC discontinued the product because "the transvaginal approach created concerns related to infection from the direct path through the vagina."[169] Again, BSC's Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Prefyx, Pinnacle, and Uphold products also present the same issues with transvaginal placement. Finally, BSC discontinued the Protegen product because of concerns with mesh erosion: "[t]he rate of vaginal erosion was higher than our acceptable standard of performance."[170] Despite BSC's acknowledgment that the Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Prefyx, Pinnacle, and Uphold products cause the same erosion problems as the Protegen,[171] BSC thereafter continued to market the Mesh Products.

In a document dated April 22, 1999 describing BSC's decision to voluntarily discontinue the Protegen sling, BSC pledged, "[i]n connection with any future sling materials, BSC will gather clinical data to assess product performance in a broad spectrum of clinical situations."[172] BSC chose not to assess the performance of its future slings in clinical situations, including the Advantage, the Advantage Fit, Lynx, Solyx, and Obtryx slings.[173] Nor did BSC study the Pinnacle or Uphold devices in a clinical setting for safety or effectiveness. In fact, the director of Clinical Department at BSC, Janice Connor, testified that no one at BSC told her about this plan for future vaginal mesh products.[174] In my opinion, to a reasonable degree of medical and scientific certainty, BSC did not follow its own internal guidelines developed from the Protegen experience when developing the Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Prefyx, Pinnacle, and Uphold devices. In my opinion, to a reasonable degree of medical certainty, the Protegen experience shows

[167] DHS01001587.
[168] BNGO1000262.
[169] *Id.*
[170] BSCM06500000261.
[171] Miragliuolo Dep. (Vol. 1) 389:10-11; BSCM07400021988-89.
[172] *Id.*
[173] Connor Dep. (Vol. 1) 103:3-104:7.
[174] Connor Dep. (Vol. 1) 208:20-209:5; *See also* Dep. of Alfred Intoccia 143:13-19.

the types of complications that transvaginal mesh made of synthetic materials, like the Mesh Products, can cause after permanent implantation in the human body.

D. BSC Made Public Claims About The Properties And Safety Of The Mesh Products To Physicians And Patients Through Marketing Materials That Lack Support From The Available Medical And Scientific Literature.

I also reviewed BSC documents and have the opinion, to a reasonable degree of scientific and medical certainty, that many of the medical and scientific facts contained therein are not supported by the available medical or scientific literature. Recall, BSC neglected to conduct adequate premarket testing and appropriate clinical trials (pre- or post-market). Nevertheless, BSC made clinical representations about the safety, performance, and effectiveness of the Mesh Products to the public (including the medical community, sales representatives, and potential customers), despite lacking factual, clinical, medical, and scientific support for the representations:

- Every DFU for the Mesh Products claims to provide the clinical risks associated with the products. However, with the exception of the Prefyx, BSC neglected to determine the risks associated with the Mesh Products in clinical studies before marketing them.[175] Except the Prefyx, BSC provided all Mesh Products without any clinical evidence to substantiate the claimed risks with the products. Nor could BSC provide the complete risk profile associated with the Mesh Products because BSC did not determine risks of all Mesh Products, except the Prefyx, in clinical studies before market. Ultimately, BSC provided inadequate DFUs with all Mesh Products.
- In a March 19, 2001 email entitled "Melting of Mesh Tang Using Hot Iron," BSC claims de-tanging of the suburethral portion of the Advantage, Advantage Fit, Lynx, Obtryx, Prefyx, and Solyx slings "will reduce the risk of potential erosion, if any, after placement under urethra." BSC perpetuated this benefit while marketing each of the sling products. BSC never gathered clinical evidence, nor does any otherwise exist, on whether de-tanging decreased the risk of erosion. Nor did BSC disclose the effect of melting polypropylene on degradation.[176]
- The de-tanging or deburring is further discussed in an email of May 15, 2001, providing the "reason for the deburring is to prevent erosion of the urethra and vagina."[177]

[175] Gardner Dep. 19:9-13; Sherry Dep. 100:10-16.
[176] BSCM07400006570.
[177] BSCM07400008173.

However, BSC decided against testing whether the detanged portion of the mid-urethral slings resulted in more clinical benefits or fewer clinical risks than mesh with tangs.[178] BSC did not provide clinical evidence to support the claimed reduced erosion risk with detanging, nor was any evidence otherwise available to substantiate the claim.

- In the development summary for Pinnacle mesh (later renamed Advantage mesh) by Jamie Li dated July 27, 2001, BSC chose the material used in the Pinnacle mesh (later Advantage, Advantage Fit, and ultimately the Lynx, Obtryx, Prefyx , Solyx devices) "due to the excellent tissue compatibility and clinical outcomes of monofilament polypropylene meshes." BSC does not provide evidence of the statement in this email.[179]
- In an August 3, 2004 PowerPoint presentation entitled Meshology 101, BSC trained representatives on selling the Advantage mesh at a summer training conference. One slide, entitled Selling the Advantage Mesh, lists the following sales points: greater resistance to deformation; designed to minimize tissue irritation to the urethra and vaginal mucosa (instructed to present with passion); and polypropylene is non-reactive *in vivo*, which minimized the risk of chronic inflammation and infection. No data is presented to justify these claims and I am aware of no scientific or medical support for these statements.[180]
- In a December 29, 2010 email, BSC told two physicians that the Lynx suprapubic slings can be "used on all patients, are highly effective, and offer low rates of intra and post-operative complications." No data is offered to support these claims and I do not believe that these claims are supportable by the available medical and scientific literature.[181]
- In a Women's Health Portfolio brochure from 2010, BSC stated the Advantage Fit's placement in closer proximity to the pubic bone reduces the potential chance for bowel or bladder injury. BSC provides no clinical support for this claim.[182]
- In a 2006 brochure entitled Women's Health Sales Training Program, BSC claimed that Advantage mesh is a proven material with a long history of compatibility.[183] BSC

[178] Connor Dep. (Vol. 3) 165:21-166:23.
[179] BSCM07400002132.
[180] BSCM09300093946.
[181] BSCM09300000001.
[182] Dep. of Maya Matusovsky (Exhibit 393).
[183] BSCM06300021197, at p. 20.

also claimed that the protective sleeve around the Advantage mesh enables free floating, which absorbs the tensioning load.[184] No data, in BSC's possession or otherwise, supported these assertions. Furthermore, BSC did not disclose the presence of a chronic inflammatory reaction after implantation nor the polypropylene supplier's admonition against permanent implantation in humans.

- The DFUs provided with the Pinnacle products after clearance indicated use for surgical treatment of POP in posterior, apical, and anterior repairs.[185] Almost four years later, however, at least one BSC employee acknowledged, the literature contained "[n]ot enough data to support [the indicated] posterior" use of the product for surgical treatment of POP.[186]
- In BSC's 2008 patient guide for POP treatment, BSC described surgical treatment with mesh as a dramatically advanced and newly favored treatment option:[187] ". . . [i]n recent years, dramatic advances have been made in the surgical treatment of [POP];"[188] "[i]n recent years, general trends have favored vaginal repair techniques - as they often provide excellent outcomes."[189]
    - BSC's patient guide contained no clinical evidence that showed mesh provided excellent outcomes for POP or established mesh as a dramatic advancement in the treatment of POP. Because BSC never studied its POP products in a clinical trial and the literature lacked any publications on the Pinnacle or Uphold until the end of 2009,[190] no clinical evidence existed in 2007, 2008, and most of 2009 to support BSC's claims about the efficacy of POP products.
    - In addition, BSC's 2011 "Pelvic Floor Repair Literature Summary" contradicts BSC's claim: "[s]ynthetic mesh-augmented repair of posterior vaginal wall prolapse . . . did not significantly improve success rates when compared with traditional posterior colporrhaphy."[191] Further, "[d]ata regarding graft use for

[184] *Id*. at 26.
[185] BSCM00800003045, at -047 (anterior / apical); BSCM00800003551, at -053 (anterior / apical & posterior).
[186] BSCM06100034693.
[187] BSCM01900011105.
[188] *Id*. at -104.
[189] *Id*. at -108.
[190] Connor Dep. (Vol. 2) 328:20-330:24; Connor Dep. (Vol. 3) 77:22-78:7; BSCM05100112164; *see also* Connor Dep. (Vol. 3) (Exhibits 1298 &1299).
[191] BSCM06100053678, at -682; *accord* at -687.

posterior compartment repair are insufficient to determine superiority to colporapphy."[192]

- BSC's physician brochures for the Pinnacle from 2007 through 2009 told doctors the kit "include[d] custom enhancements of proven technology."[193] However, because no clinical evidence on the Pinnacle's safety and effectiveness for human use existed until 2010,[194] BSC's description of the Pinnacle as a "proven technology" in 2008 and 2009 lacked any evidentiary basis. In fact, the lack of any clinical evidence through at least 2009 established the Pinnacle as an unproven technology in 2007, 2008, and 2009. Moreover, the clinical "evidence" released after 2009 on the Pinnacle is still insufficient to prove safety and effectiveness for human use. BSC's claims in 2007, 2008, and 2009 lacked clinical support not only then, but also today.
- The 2007-2008 Pinnacle brochure informed physicians that BSC configured the Pinnacle with *the* mesh with "the **greatest** history of success": "Polyform Mesh is made from uncoated monofilament microporous Polypropylene. This material has the **greatest** history of success and has been implanted throughout the body for over 30 years."[195] BSC scaled back the language in the 2008-2009 brochure, without portraying the Pinnacle as the mesh with "the greatest history of success": "Polyform Mesh is made from uncoated monofilament microporous Polypropylene. This material has had a history of success in various parts of the body for over 30 years."[196]
  - As an initial matter, because the FDA cleared polyform for use on June 17, 2005, the historical use of Polyform spanned less than three years when BSC made claims about its 30-year history to doctors in the 2007 Pinnacle brochure.[197]
  - Next, without any clinical evidence on the Pinnacle's effectiveness through at least 2009, no basis existed for BSC to claim the mesh used in the Pinnacle had "greatest history of success," or much less, any history of clinical success. Indeed, in the citation for the 30-year historical claim from a 2009 brochure, BSC even admits the

[192] *Id.* at -687.
[193] BSCM05100024369, at -370 (2007-2008 version); BSCM06300006616, at -617 (2008-2009 version).
[194] BSCM05100112164
[195] BSCM05100024369, at -371 (emphasis added).
[196] BSCM06300006616, at -618.
[197] BSCM05100000391.

claim "may not be indicative of clinical results" because BSC based the claim on bench testing in 2005.[198]

- In the 2009 brochure for the Uphold, BSC claimed it "designed" the Uphold "to reduce the risk of erosion."[199] BSC declared this potential Uphold benefit without citation to any evidence. BSC's statement requires a comparative analysis to determine whether Uphold carries a different risk of erosion than another product.[200] However, BSC launched all Mesh Products without clinical studies that compared the safety and effectiveness of its products to other manufacturer's products.[201] In 2012, the literature still lacked support to claim the Uphold carried less risks than other procedures because the clinical studies available then did not establish the Uphold's safety and effectiveness in a comparative study with another procedure.[202] In fact, the need for a comparative study involving the Uphold was "critical" in 2012.[203]

In my opinion, to a reasonable degree of medical and scientific certainty, many of BSC's representations about the Mesh Products are not supported by the available medical and scientific literature. Furthermore, BSC has not identified any internal testing or studies that establish the accuracy or basis for these representations. Without adequate medical or scientific foundation, these representations cannot be considered reliable, true or accurate in any way.

E. The Directions For Use ("DFU") BSC Provided With All Mesh Products Do Not Fully Disclose Or Adequately Warn About The Mesh Products' Known Or Knowable Risks, Adverse Reactions, And Characteristics.

A medical device manufacturer provides a DFU with a product to equip physicians with information necessary to decide whether to treat a particular patient with the device. The DFU also provides physicians instructions for using the device. In addition, the DFU discloses the device's known or knowable adverse reactions and risks so the physician can relay the risks to the patient and reach an informed decision on whether to use the product. To make an informed decision on whether to use a product, the DFU must warn physicians about not only potential adverse events associated with the device, but also the frequency, severity, duration, and potential permanence of

[198] Connor Dep. (Vol. 1) (Exhibit 473, at 4 n.7)
[199] BSCM04100000073, at -074.
[200] Connor Dep. (Vol. 4) 476:20-478:20.
[201] *Id.* 408:7-19.
[202] *Id.* 420:16-427:3.
[203] *Id.* (discussing Exhibit 1326).

adverse events. If a manufacturer of a medical device knows the product's design causes complications, increases the risk of complications, or presents a risk unique to the design, then the manufacturer should provide that information to physicians in a warning. If a manufacturer knows its medical device may cause chronic, severe, or permanent complications, the manufacturer should also provide that information to physicians in a warning.

Throughout my education, training, and surgical and clinical practice, I have reviewed numerous DFUs (sometimes called Instructions for Use ("IFU")) for a variety of products, including mesh products, to understand the proper use of the device and learn about the complications or adverse events associated with the device. In my clinical experience, I use DFUs extensively to learn about products and counsel patients on adverse events and risks identified in device DFUs. I have gained expertise in DFUs from my extensive clinical experience reviewing and counseling patients on DFUs, including pelvic mesh patients. I reviewed the various versions of DFUs for BSC's Mesh Products, including the Advantage, Advantage Fit, Lynx, Obtryx, Prefyx, Solyx, Pinnacle, and Uphold. I also reviewed the all physician brochures ever in circulation for BSC's Mesh Products. In addition, I reviewed several iterations of patient brochures for BSC's Mesh Products, including the brochures for the SUI products and POP products.

In my opinion, to a reasonable degree of medical certainty, BSC provided inadequate warnings with all BSC Mesh Products:

- As of 2015, no BSC-sponsored RCT existed for BSC to verify the safety and effectiveness of all Mesh Products.[204] As of 2015, no BSC-sponsored clinical studies existed to verify the safety and effectiveness of the Advantage Fit, Lynx, Solyx, Pinnacle, and Uphold.[205] Except for the Prefyx, BSC launched every all Mesh Products without clinical data on safety and effectiveness for human use.[206] In the first Pinnacle DFU, and all DFUs for the Advantage, Advantage Fit, Lynx, Solyx, Prefyx, and Obtryx, BSC chose not to warn physicians that BSC does not know if the devices are safe or effective for human use because BSC decided not to verify whether the devices were safe and effective for human use in an RCT.

[204] Connor Dep. (Vol. 1) 101:15-104:7; Connor Dep. (Vol. 3) 65:21-71:21, 73:7-74:3, 77:17-78:7, 244:21-25.

[205] Connor Dep. (Vol. 3) 65:21-71:21, 73:7-74:3, 77:17-78:7.

[206] *Id.* 80:3-81:4.

- All DFUs for the Mesh Products contain inadequate "Contraindications" sections. Specifically, BSC provided inadequate "Contraindications" in the DFUs of all Mesh Products because the DFUs do not contain certain patient selection criteria that physicians should consider before implanting these devices.
- The DFUs state that the "physician is advised to consult the medical literature regarding techniques, complications and hazards associated with the intended procedures." However, insufficient information exists in the literature, as discussed above, on techniques, complications, and hazards associated with the Mesh Products. BSC's DFUs do not warn physicians that the available scientific literature contains insufficient evidence to establish whether the Mesh Products are safe and effective for human use. BSC's DFUs do not warn physicians that the available scientific literature lacks adequate information on the techniques, complications, and hazards associated with the Mesh Products.
- The Mesh Products' DFUs do not sufficiently or adequately advise physicians on the permanence, frequency, or severity of the complications that can arise from the use of the devices. Specifically, the DFUs do not warn physicians that potential complications can be permanent, future procedures and surgeries may not resolve the complications, or complete removal of the devices may be surgically impossible.
- The Mesh Products' DFUs do not inform the physician that the devices can chemically and biologically degrade, shrink, contract, rope, curl, fold, flake, crack, embrittle, stiffen, harden, elongate, or otherwise alter inside the human body.
- The DFUs do not warn physicians that BSC configured the devices with polypropylene that was not intended for use as a permanent implant in the human body.
- The DFUs do not inform physicians that some publications in the limited medical and scientific literature recommend using other manufacturers' products or procedures to treat SUI or POP due to dangerous complications associated with the Mesh Devices.
- The Mesh Products' DFUs do not inform physicians that a woman's tissue responses to BSC's meshes can induce a greater foreign body, enhanced inflammatory response, excessive scarring, multiple erosions that persist for life, chronic and debilitating pelvic pain and new pain syndromes, recurrence, worsening or *de novo* incontinence, chronic and permanent dyspareunia, new infections, rejection of the mesh, permanent sexual

dysfunction, defecatory dysfunction, vaginal scarring; wound healing problems, or injury to ureters, bladder, and urethra.

– BSC admits occurrence rates for adverse events were not disclosed in their brochures or DFUs.[207]

All the omitted warnings are relevant to physicians when conducting a risk-benefit analysis or determining the appropriate use of the Mesh Products. None of the omitted warnings are commonly or well-known in the medical community. In my opinion, physicians required all the omitted information to obtain true informed consent from patients and make appropriate treatment recommendations to patients. In the absence of the material, relevant, and compelling warnings that BSC omitted from the DFUs, BSC revoked patients' abilities to properly consent to the implantation of a permanent medical device.

F. The Severe, Debilitating, And Life-Changing Complications Associated With The Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Prefyx, Pinnacle, and Uphold Products Outweigh The Products' Benefits.

It is my opinion, based on my training, experience, and extensive review of the literature and BSC's internal documents that the severe, debilitating and life changing complications associated with the Mesh Products outweigh the benefits, if any, of the medical devices. In my clinical experience and practice, a substantial number of women implanted with the Mesh Products present with chronic and debilitating complications, including erosions and pain, that will continue indefinitely. The chronic, debilitating, and permanent complications caused by the Mesh Products outweigh the potential benefits of improving a patient's quality of life. With alternative, traditional surgeries factored into the risk-benefit calculus, the Mesh Products' benefits weigh even less because traditional surgeries involve complications that occur at lower frequencies and with less severity than the complications associated with the Mesh Products. With traditional suture based surgeries, patients avoid risks unique to the Mesh Products' polypropylene mesh like mesh degradation, contraction, shrinkage, and clinically significant erosion. The scientific literature reports that mesh erosion with polypropylene products occurs at high rates.[208] Although traditional

[207] Gardner Dep. 68:15-18; Sherry Dep. 168:16-20.

[208] In 2010, *Iglesia* et al reported a 15.6 mesh erosion rate with a dismal 40.6% cure rate. Iglesia et al., *Vaginal mesh for prolapse: a randomized controlled trial*, 116 (2 Pt. 1) OBSTET. GYNECOL. 293-303 (2010). In 2011, *Withagen* reported a mesh erosion rate of 16.9% and again in 2010, *Nieminen* reported a mesh erosion rate of 19%. Withagen et al., *Trocar-guided mesh compared with conventional vaginal repair in recurrent prolapse: a randomized controlled trial*, 117 (2 Pt. 1) OBSTET. GYNECOL. 242-50 (2011); *see also* Nieminen et al., *Outcomes after anterior vaginal wall*

surgeries can cause symptoms such as pain and dyspareunia following surgery, the chronic pain and dyspareunia associated with the Mesh Products involve greater extents, longer durations, and more risk and severity than traditional surgeries. In addition, traditional surgeries do not result in untreatable complications and symptoms that result the Mesh Products.

Although several recent studies and publications involve polypropylene mid-urethral slings, unfortunately, most lack quality designs and suffer from biases that dilute their information about the long-term, severe, and debilitating complications generally associated with the Mesh Products. In fact, the medical and scientific literature contains no publications on long-term RCTs with safety as the primary endpoint for any of BSC's polypropylene devices, including the Mesh Products.[209] A recent Cochrane Review on mid-urethral slings found the follow-up period short for most trials and qualitative issues with the available evidence.[210] Few trials reported outcomes beyond a year. The review could not reach any conclusions from the data on long term adverse effects. Only a handful of long-term RCTs involve polypropylene mid-urethral slings, but the primary endpoints of effectiveness – rather than safety – in these RCTs preclude discovery of major and long-term complications. Although registries or databases present a more likely vehicle to determine true incidences, the designs of published registries monitor short-term complications and ignore some complications such as dyspareunia or pain.[211]

In my opinion, to a reasonable degree of medical certainty, the BSC-sponsored registry for the Advantage and Obtryx products was not adequate to provide any reliable information concerning the devices' safety or effectiveness for human use.[212] BSC's own representatives acknowledge registries provide less reliable data than RCTs: "[a] registry is a less structure. There's typically less data collected, less follow-up visits, less assessments performed, and there are no randomized choices of procedures. The physicians along with the patient make the decision

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repair with mesh: a randomized, controlled trial with a 3 year follow-up, 203(3) AM. J. OBSTET. GYNECOL. 235e1-8 (2010).

[209] Connor Dep. (Vol. 3) 204:6-10.

[210] Ogah et al., *Minimally Invasive Synthetic Suburethral Sling Operations for Stress Urinary Incontinence in Women: A Short Version Cochrane Review*, 30 NEUROL. URODYN. 284-91 (2011).

[211] Tamussino et al., *Tension-Free Vaginal Tape Operation: Results of the Austrian Registry*, 98 OBSTET. GYNECOL. 732-36 (2001); Tamussino et al., *Transobturator tapes for stress urinary incontinence: Results of the Austrian registry*,197 AM. J. OBSTET. GYNECOL. 634.e1-e5 (2007); Kuuva et al., *A nationwide analysis of complications associated with the tension-free vaginal tape (TVT) procedure*, 81(1) ACTA. OBSTET. GYNECOL. SCAND. 72-7 (2002); Caquant et al., *Safety of Trans Vaginal Mesh procedure: Retrospective study of 684 patients*, 34(4) J. OBSTET. GYNAECOL. RES. 449-56 (2008); Dykorn et al., *TVT compared with TVT-O and TOT: results from the Norwegian National Incontinence Registry*, 21(11) INT. UROGYNECOL. J. 1321-26 (2010).

[212] BSCM04800008700; BSCM04800009884; BSCM04800009917; (BSCM12600008840.

as to what procedure a patient might undergo."[213] Of all BSC's Mesh Products, the Prefyx was the only other device BSC monitored in a registry.

BSC began a registry for the Obtryx and Advantage, giving the marketing group at BSC a "little oversight."[214] The registry enrolled a total of 2,015 patients. 1,517 Obtryx patients and 479 Advantage patients comprised the original cohort, whittling the cohort to 1,996 patients. The registry prospectively monitored and evaluated voiding status, stress test, overall continence status if available at discharge, three months, and twelve months. The registry lost 363 Obtryx patients and 122Advantage patients to follow-up. A total of 1,511 completed the full twelve month evaluation.[215] While 98.8% of patients at hospital discharge (1620/1639) reported no pain or normal pain, the long term data revealed a different outcome. In the Obtryx arm, "57.7% (875/1517) of patients reported at least 1 adverse event," with 656 patients reporting "any pain" (the most common complaint regardless of device causality or association).[216] Six (6) patients reported ongoing pain at twelve months, and fifteen (15) patients reported dyspareunia through twelve months.[217] Six (6) patients experienced vaginal tape extrusion.[218] In the Advantage arm, four (4) patients experienced vaginal tape extrusion at twelve months. A total of 48.4% of patients reported at least one adverse event, with 171 patients (35%) reporting "any pain."[219]

The registry generated limited data and contained numerous reporting errors.[220] Despite the errors, BSC presented and distributed the data to physicians.[221] Specifically, BSC presented the data to physicians at seminars:

- **European Association of Urology's Annual Congress**, March 21-24, 2007 (Berlin, Germany). Dr. Costa presented the data in an abstract entitled, "First International Registry on Sub-Mid Urethral Tapes (M.U.T.) Implanted By Retro Pubic or Transobturator Route: Preliminary Results on 900 Patients." BSC turned this presentation into a marketing document with the PSST number MVU6830.[222]

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[213] Connor Dep. (Vol. 1) 226:14-24, 227:1-2.
[214] *Id.* 228:5-15.
[215] BSCM05200049005; BSCM05200048906.
[216] BSCM05200048906.
[217] *Id.*
[218] *Id*.
[219] *Id*.
[220] BSCM04800002326; BSCM04800003230; BSCM04800003553; Connor Dep. (Vol. 1) 234:21-24, 235:1-19.
[221] Connor Dep. (Vol. 1) 242:4 - 245: 8.
[222] BSCM04800093622; BSCM06300021917; BSCM06300021918.

- **39th Global Congress of Minimally Invasive Gynecology (AAGL) Annual Congress**, November 8-12, 2010 (Las Vegas, Nevada). Dr. Costa presented the registry data in an abstract entitled, "Comparisons of Safety and Efficacy of the Obtryx Sling and Advantage Mid-Urethral Sling for the Treatment of Stress Urinary Incontinence: Propensity Matching Results in a Large International Registry."[121] This presentation presented data collected at three and twelve-month follow-ups. BSC turned this presentation into a marketing document, with the PSST number MVU13230.[223]

Peer reviewed journals criticized and rejected the abstracts and registry data that Dr. Costa presented to physicians as safety and effectiveness evidence:

- ***Journal of Urology***: **Rejected** [September 2009][224]
  - "Unacceptable low follow-up rates. Only 808 patients were evaluated at 12 months. This is only 51% of the initial population . . . . With a low % of patient follow up, then the study is subject to selection bias with unhappy patients or patients with adverse events going elsewhere"
  - "Implausible adverse event results. Table 3 reports that only 8 of 1579 subjects (0.5%) reported a UTI in the 12 month period following a mid-urethral sling! In well designed surgery trials with careful follow-up, as much as 40% of subjects will develop UTI's in the first 2 years after incontinence surgery (Albo et al, NEJM, May 21, 2007). This 0.5% UTI rate is so far below the range of plausibility that it brings into question the possibility of gross under-reporting for other adverse events and it raises questions about the credibility of the entire registry and thus the validity of this entire study."
- ***British Journal of Urology International***: **Rejected** [October 2012].[225]
  - Patients lost to follow up is "huge"- "company sponsored, bias in selection, total patient numbers are not matching in the results , short follow- up.
- ***International Urogynecology Journal***: **Rejected** [June 2012][226]
  - "Materials and methods: The sample size is relatively large, although not really outstanding considering the study design. Follow-up duration is, however, short."

[223] BSCM11200016681; BSCM06100066390.
[224] BSCM04800001142.
[225] BSCM12800016718.
[226] BSCM04800085009.

- "The title is appropriate. An alternative to consider would be to use 'One year Follow-up of' rather than 'Safety and Efficacy of,' since we know that there are potential outcomes with slings that extend beyond 1-year that impact safety and efficacy."
- From the editor: "[w]hile there are some positive and negative comments from the reviewers, the shorter-term follow-up and lack of objective outcome measures . . . are of concern. As with all registeries [sic], reporting is voluntary and it isn't clear how many patients with poor outcomes were not included."
- Also in the rejection emails, BSC employees discussed submitting the paper to a lower-tier journal to ensure publication: "[t]he alternative would be to try to talk Costa into a very low-tier journal with a higher chance of acceptance, but I think he might be resistant to that from a prestige standpoint."

These criticisms from the peer-review process illustrate qualitative weakness of the studies BSC relies on to support claims of safety and effectiveness. Specifically, the void of peer-reviewed publications that present the true incidence and nature of long-term and life-altering complications, without inherent biases, negates or degrades the value of the large majority of the studies.

I have extensively reviewed and analyzed the studies. I am prepared to discuss the studies including the small number of studies that tracked chronic pain, dyspareunia, and erosions on a long-term basis. Polypropylene transvaginal mesh causes not only dyspareunia, but also chronic and permanent dyspareunia. *Shah* and *Badlani* found the overall incidence of dyspareunia in patients undergoing a SUI or POP surgery with transvaginal polypropylene mesh at up to 6.2% and 24.4% respectively.[227] The scientific literature attributes dyspareunia to mesh erosion, infection, shrinkage and contraction, and extensive scarring and fibrosis.[228] The authors also reported on chronic pelvic pain in patients after POP surgery with transvaginal polypropylene mesh, ranging between 1.2% and 24% in the literature.[229]

The Abbott (2014) study is also particularly noteworthy. Abbott described a series of 347 patients evaluated from 2006 through 2010 for mesh related complications. Approximately 50% had a sling only and an additional 26% had a sling and TVM mesh. The median time from

[227] Shah et al., *Mesh complications in female pelvic floor reconstructive surgery and their management: A systematic review*, 28(2) IND. J. UROL. 129-153 (2012).
[228] *Id.*
[229] *Id.*

placement to evaluation was 5.8 months with a range of 0 – 65.2. This means that RCTs or registries with less than twelve-month follow-ups would not capture many of the patients and data collected in Abbott. Also only 26% of patients received care at another facility before attending one of the study sites, meaning the implanting physicians did not know about 75% of these complications, again highlighting the limited utility of data at the primary site. The authors found 30% of patients with dyspareunia, 43% with erosion, and 35% with pelvic pain.[230] This study highlights the degree and severity of the complications that mesh slings like the Advantage, Advantage Fit, Lynx, Obtryx, Solyx, and Prefyx cause and, importantly, that physicians in the real world simply do not know about the severity of the problem. As BSC noted during Dr. Mickey Karram's presentation, "[a]t the end of the day, people who use mesh or don't, have little guidance on what they should do clinically."[231] This is why, in my opinion to a reasonable degree of medical and scientific certainty, it is extremely important for manufacturers of SUI and POP products, like BSC's Mesh Products to accurately and fully report the risks and complications associated with the mesh devices to doctors – something BSC simply has not done.

G. BSC Polypropylene Mesh Removal Requires A Difficult And Sometimes Impossible Surgery With A High Likelihood Of Injuring Surrounding Tissue.

Regardless of the compartment where BSC's polypropylene mesh is placed for prolapse, there is no reduction in the reoperation rates for prolapse.[232] In fact, the reoperation rates following initial mesh repair has increased in my clinical experience and practice. In addition, the complications associated with BSC's Mesh Products result in more severe, frequent, and difficult to treat complications due to the mesh being a permanent implant.[233]

Thus, permanence presents another significant and potentially catastrophic problem with BSC's Mesh Products because they unfortunately do exactly what they were designed to do, stay forever. The polypropylene mesh becomes embedded and cemented into the body making removal

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[230] Abbott et. al., *Evaluation and management of complications from synthetic mesh after pelvic reconstructive surgery: a multicenter study*, 210(2) AM. J. OBSTET. GYN. 163e.1-8 (2014).

[231] BSCM04800072360.

[232] Maher et al., *Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse*, Issue 2 COCHRANE DATABASE SYSTEMATIC REVS. CD012079 (2016).

[233] In 2010, *Clave et al.*, performed a comparative analysis of 100 explants of polypropylene mesh and concluded it is not inert. In his study Clave found that all 100 explants showed evidence of degradation on scanning electron micrograph after three months. In this study mesh damage included superficial degradation with peeling of the fiber surface, transverse cracks in the implant threads, significant cracks with disintegrated surfaces and partially detached material and superficial and deep flaking. Furthermore he found that polypropylene implants degraded more in the presence of infection or inflammation, processes that are frequently found in mesh implants. Clave (2010).

virtually impossible to completely surgically extirpate. In the event of complications with BSC's Mesh Products, no specific "exit strategy" exists for surgeons. Moreover, even multiple operations may not end the patient's suffering and complications.

From my perspective as a surgeon and in my clinical experience, removal surgeries evoke frustration and disappointment because we want to help our patients, but the nature and difficulties in locating and completely removing polypropylene mesh can preclude satisfactory results for patients. BSC did not proactively alert physicians, either in the DFUs or in their direct communications, that if complications with the Mesh Products require removal, surgeons may encounter serious difficulty finding the line of demarcation for complete removal.[234] It is very important that surgeons are able to visualize the edge of demarcation, or where the mesh ends and/or begins so that they are able to remove all mesh if necessary to adequately treat the patient. Inability to visualize the implanted mesh could complicate the surgeon's ability to remove it. BSC has had no trials designed exclusively to assess mesh removal.[235] Patient safety and wellbeing should always be at the forefront for BSC and if a patient is unable to have her mesh fully removed, that could cause long-standing, lifelong potential complications, including further chronic and/or permanent pain and risk of infection. Complications with all BSC Mesh Products, including those for treatment of POP and SUI, can require removal surgeries. Unfortunately, these mesh systems stay forever; they were always intended to be permanent devices. The mesh becomes embedded into the body making it virtually impossible to completely surgically eliminate when it has to be removed. There is simply no acceptable exit strategy for these mesh devices. Even after twenty years of polypropylene mesh use in the female vagina and pelvic floor, no validated, reliable, and scientifically proven method exists to treat complications when they arise or remove the mesh implant.

In 2010, a BSC sponsored pre-clinical animal study designed to evaluate the potential visualization differences between color of mesh. The study demonstrated that visualization of Pinnacle Lite blue mesh was easier and more accurate than the Mesh Products configured with white mesh.[236] Dr. Miller, the Pinnacle inventor, found "[e]dge demarcation is a critical difference between the natural colored and blue colored mesh. Accurate location of device edges is required

[234] Connor Dep. (Vol. 1) 35:11–36:6.
[235] Connor Dep. (Vol. 1) 38:15 – 38:24
[236] BSCM048000058558.

for complete removal of device."[237] The Mesh Products remained on the market for years following the findings of this study, and the color remained unchanged during this time.[238] Later BSC products incorporated the blue color change.[239]

V. CONCLUSION

BSC marketed and sold the Mesh Products despite numerous characteristics that make them unsuitable for implantation in a woman's vagina. Some of the characteristics include the following: (1) degradation of the mesh; (2) small pores and heavy weight; (3) chronic foreign body reaction; (4) fraying and particle loss; (5) Infections and Biofilms; (6) roping and curling of the mesh; (7) loss of pore size with tension; (8) fibrotic bridging leading to scar plate formation and mesh encapsulation; and (9) shrinkage / contraction of the encapsulated mesh.

BSC not only marketed Mesh Products that should never be implanted through the vagina, but also failed to inform physicians and patients about known, pre-launch risks associated with the devices. BSC's warning choices robbed women of the ability to make an informed decision with their physicians about whether to consent to a permanent medical implant. Despite possessing evidence of potential toxins in the Mesh Products, BSC never informed physicians or patients about the devices' possible toxicity in women. Finally, BSC used promotional materials to market the Mesh Products without disclosing key conflicts of interest, true complications, and complication rates.

As a result of these failures as fully set forth in this report, the Advantage, Advantage Fit, Lynx, Obtryx, Solyx, Prefyx, Pinnacle, and Uphold products caused and will continue to cause a multitude of injuries in women, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, dyspareunia that can be chronic, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and / or the need for additional surgeries, among others.

I reserve the right to amend and / or supplement this report if new discovery or facts necessitate amendment or supplementation.

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[237] Connor Dep. (Vol. 1) 63:1-64:20; BSCM048000058558.
[238] Connor Dep. (Vol. 1) 68:10-69:23.
[239] Connor Dep. (Vol. 1) 74:1-64:11.

Dated this 4th day of June, 2018.

Bruce A. Rosenzweig, M.D.